Tampere University

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With a focus on prehospital traumatic brain injury

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ACADEMIC DISSERTATION
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ABSTRACT

Out-of-hospital emergency medical services (EMS), also known as prehospital EMS, typically refer to the delivery of medical care at the site of the adverse medical event.

The first physician-staffed EMS-unit in Finland was introduced in the year 1972 in Helsinki. During the 1980's other physician-staffed EMS units were founded and the first physician-staffed helicopter emergency medical service (HEMS) unit was introduced in 1992.

As EMS systems and prehospital care are difficult to evaluate, the true efficacy and value of such systems are difficult to determine. This thesis evaluates the impact of physician-staffed EMS on patient outcome with a focus on prehospital traumatic brain injury (TBI).

The thesis is based on four original publications. The first studied the long-term outcome of 483 critically ill or severely injured patients treated on-scene by EMS physicians over a five-year (2007-2011) period (I). The patients' one-year mortality was 35 % and good neurological recovery (defined as the ability to live an independent life) was found in 55 % of the patients. After the incident, 85 % of the long-term survivors as well as most of the patients in the younger age groups (below 60 years of age) recovered well neurologically.

To evaluate the role of EMS physician involvement, the prehospital treatment and outcomes of patients with severe TBI from 2005-2010 and 2012–2015 in two study locations (the Helsinki and Uusimaa region and in Pirkanmaa region in Finland) were determined in three different scenarios: paramedic- versus physician-staffed EMS (II), before and after the introduction of physicians into paramedic EMS (III) and pooled data considering the effect of an on-scene physician on the TBI patients' outcome (IV). The data covering 2011 were excluded as a physician-staffed HEMS was implemented in the Pirkanmaa Hospital District that year and had a significant impact on the local EMS.

When two regions with differently structured EMS systems were compared, the mortality was lower with EMS physician present on-scene, and the EMS system without EMS physician remained as a risk factor for mortality in the multivariable analysis after the patients were adjusted by age (II).

The results also show better neurological outcomes in patients treated by EMS physicians, and in a univariate analysis of EMS physicians, a lower age and secured airway were associated with good neurological outcomes (III).

Based on these findings, the gathered TBI patient data were further analysed with a binary logistic regression analysis (IV) as the mortality data for 651 patients and neurological outcome data for 634 patients were available for analysis.

In the univariate analysis, increasing age, lower on-scene Glasgow Coma Scale (GCS) and prehospital treatment without the presence of EMS physicians were factors associated with higher mortality. In a multivariable analysis, these variables, with the addition of hypotension, remained significant factors for mortality.

Factors associated with good neurological outcomes in the univariate analysis were lower age, higher on-scene GCS and the presence of an on-scene EMS physician. In the multivariable analysis, all these factors remained significant for good outcomes, while hypotension was associated with poor outcomes.

Based on these studies, the following conclusions can be drawn: The overall prehospital one-year mortality of critically ill or severely injured patients treated on-scene by EMS physicians can be considered low, and prehospital on-scene EMS physicians treating severe TBI patients is associated with lower mortality and better neurological outcomes.

TIIVISTELMÄ

Ensihoidolla tarkoitetaan äkillisesti sairastuneen tai loukkaantuneen potilaan kiireellistä hoitoa ja kuljettamista jatkohoitoon. Suomen ensimmäinen lääkäriyksikkö perustettiin Helsingissä vuonna 1972. 1980-luvulla lääkäriyksikkötoiminta laajeni ja ensimmäinen lääkärihelikopteri aloitti toimintansa vuonna 1992.

Ensihoitoa sekä ensihoitojärjestelmän että sen osien toimintaa ja toiminnan tehokkuutta on haastavaa tutkia. Tämän väitöskirjan tavoitteena oli arvioida ensihoitolääkärin vaikutusta potilaan ennusteeseen ja erityisenä tutkimuskohteena olivat aivovammapotilaat.

Väitöskirja koostuu neljästä osatyöstä, joista ensimmäinen käsitteli äkillisesti sairastuneen tai loukkaantuneen potilaan hoitoa ja ennustetta viiden vuoden (2007-2011) ajanjaksolla (I). Tutkimuskohteena oli ensihoitolääkärin hoitamien 483:n äkillisesti sairastuneen tai loukkaantuneen potilaan pitkäaikaisennuste. Vuoden kestäneen seurantavaiheen aikana potilaiden kuolleisuus oli 35 % ja hyvään neurologiseen lopputulokseen (määriteltynä paluuna itsenäiseen elämään) toipui 55 % potilaista. Eloonjäänneistä 85 % ja valtaosa nuorista ikäryhmistä (määriteltynä alle 60 vuotiaat) toipuivat hyvin.

Kolme muuta osatyötä keskittyvät aivovammapotilaisiin ja ensihoitolääkärin vaikutuksen arvioimiseksi vakavien aivovammapotilaiden hoito ja toipuminen selvitettiin kahdesta tutkimuskohteesta (Helsingin ja Uudenmaan sekä Pirkanmaan alueelta) vuosilta 2005-2010 ja 2012-2015 kolmessa eri asetelmassa: ensihoitojärjestelmä ilman ja ensihoitolääkärin kanssa (II), ennen ja jälkeen-asetelma (III) sekä kohteessa olleen ensihoitolääkärin vaikutus (IV). Vuoden 2011 tietoja ei sisällytetty mukaan tutkimuksiin johtuen Pirkanmaan lääkärihelikopterin aloituksesta vuonna 2011 ja sen aiheuttamasta vaikutuksesta paikalliseen ensihoitojärjestelmään.

Kahden alueen erityyppisesti järjestettyjen ensihoitojärjestelmien vertailussa todettiin ensihoitolääkärin vähentävän vakavien aivovammapotilaiden kuolleisuutta ja monimuuttuja-analyysissä ensihoitojärjestelmä ilman ensihoitolääkäriä todettiin kuolleisuuteen vaikuttavana tekijänä, kun potilaat ikävakioitiin (II).

Tulosten perusteella myös ensihoitolääkärin hoitamien potilaiden neurologinen toipuminen on parempaa ja vakioimattomassa analyysissä ensihoitolääkäri, nuorempi ikä ja turvattu hengitystie ovat yhteydessä hyvään neurologiseen toipumiseen (III).

Edellisiin tuloksiin perustuen koottua tietoa vakavien aivovammapotilaiden hoidosta jatkoanalysoitiin binäärisellä logistisella regressioanalyysillä (IV). Kuolleisuus 651 potilaan osalta ja neurologinen lopputulos 634 potilaan osalta analysoitiin.

Vakioimattomassa analyysissa korkeampi ikä, matalampi GCS kohdattaessa ja ensihoito ilman ensihoitolääkäriä olivat muuttujia, jotka olivat yhteydessä korkeampaan kuolleisuuteen. Monimuuttuja-analyysissa nämä muuttujat sekä matala verenpaine säilyivät kuoleman riskitekijöinä.

Hyvään neurologiseen toipumiseen yhteydessä olevat tekijät olivat nuorempi ikä, korkeampi GCS kohdattaessa ja ensihoitolääkärin antama hoito. Vastaava tulos havaittiin myös monimuuttuja-analyysissa, jossa myös matala verenpaine oli yhteydessä huonoon ennusteeseen.

Väitöskirjan johtopäätöksinä voidaan todeta, että ensihoitolääkärin hoitamien äkillisesti sairastuneiden tai loukkaantuneiden potilaiden pitkäaikaisennuste on hyvä ja ensihoitolääkärin mukanaolo on yhteydessä aivovammapotilaan vähäisempään kuolleisuuteen ja parempaan ennusteeseen.

CONTENTS

ABBREVIATIONS

AED	automated external defibrillator
ALS	advanced life support
AT	activation time
BLS	basic life support
CBF	cerebral blood flow
CNS	central nervous system
CT	computed tomography
ED	emergency department
EMS	emergency medical services
EUSEM	European Society for Emergency Medicine
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Score
HEMS	helicopter emergency medical service
ICP	intracranial pressure
ICU	intensive care unit
MAP	mean arterial pressure
MICU	mobile intensive care unit
MTH	mild therapeutic hypothermia
OST	on-scene time
RSI	rapid sequence intubation
RT	response time
RTA	road traffic accident
SBP	systolic blood pressure
SOP	standard operating procedure
TBI	traumatic brain injury
TPT	total prehospital time
TT	transport time

ORIGINAL PUBLICATIONS

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals I to IV.

Publication I	Pakkanen T, Virkkunen I, Silfvast T, Randell T, Huhtala H, Yli-Hankala A. One-year outcome after prehospital intubation. Acta Anaesthesiol Scand. 2015 Apr;59(4):524-30.
Publication II	Pakkanen T, Virkkunen I, Kämäräinen A, Huhtala H, Silfvast T, Virta J, Randell T, Yli-Hankala A. Pre-hospital severe traumatic brain injury - comparison of outcome in paramedic versus physician staffed emergency medical services. Scand J Trauma Resusc Emerg Med. 2016 Apr 29;24:62.
Publication III	Pakkanen T, Kämäräinen A, Huhtala H, Silfvast T, Nurmi J, Virkkunen I, Yli-Hankala A. Physician-staffed helicopter emergency medical service has a beneficial impact on the incidence of prehospital hypoxia and secured airways on patients with severe traumatic brain injury. Scand J Trauma Resusc Emerg Med. 2017 Sep 15;25(1):94.
Publication IV	Pakkanen T, Nurmi J, Huhtala H, Silfvast T. Prehospital on-scene anaesthetist treating severe traumatic brain injury patients is associated with lower mortality and better neurological outcome. Scand J Trauma Resusc Emerg Med. 2019 Jan 28;27(1):9.

1 INTRODUCTION

The term traumatic brain injury (TBI) includes a wide spectrum of different pathologies and is characterized by a broad heterogeneity in terms of aetiology, mechanism, pathology, and severity.

The pathophysiological mechanism of TBI is traditionally divided into two phases: primary and secondary brain injury. The primary injury is the mechanical damage to the brain parenchyma at the time of impact and is the result of the initial mechanical forces. The primary injury evolves over time, reaching its peak in the following hours and overlapping with the early phases of secondary brain injury.

The secondary brain injury, originally initiated by the primary injury, takes place in the ensuing hours and days and can lead to increased mortality and disability(1). Intracranial and extracranial or systemic insults may complicate the primarily injured brain and result in secondary brain injury(2).

Worldwide, TBI is one of the leading causes of death and permanent disability, particularly in young adults(1). The prognosis of patients suffering from severe TBI depends on early support of vital functions(3, 4), and effective prehospital assessment and treatment is considered essential for good neurological recovery(5).

Hypotension, hypoxia, and hypercapnia have been shown to result in secondary brain injuries that can lead to increased mortality and disability(1). The management of severe TBI focuses on the prevention of a secondary ischemic brain injury by optimizing the balance between cerebral oxygen delivery and utilization(3, 6).

The aim of physician-staffed emergency medical services (EMS) is to supplement other EMS units in the care of prehospital patients and provide advanced care and interventions beyond the scope of standard EMS to improve the outcome of critically ill or severely injured patients.

EMS systems and prehospital care are difficult to evaluate. Accordingly, the true efficacy and value of such systems are difficult to determine(7). This thesis evaluates the impact of physician-staffed EMS on patient outcomes with a focus on prehospital TBI.

2 REVIEW OF THE LITERATURE

2.1 Prehospital emergency medical services

Out-of-hospital EMS, also known as prehospital EMS, typically refers to the delivery of medical care at the site of the adverse medical event. These systems include different services. A call centre (dispatch centre) can answer emergency calls, provide medical advice to the caller and, if necessary, dispatch a mobile medical care unit. The latter includes a vehicle that can transport medical staff to the scene and can adequately transport the patient to a health-care facility (typically named "ambulance")(8). Ambulances are the means of transportation most used and the coordination and organization of all transport is usually carried out by dispatch centres. In general all services involved in the provision of emergency medical care in an out-of-hospital setting are included in this definition(8).

Two main models of prehospital emergency care delivery exist: the Anglo-American model, which "brings the patient to the hospital," and the Franco-German model, which "brings the hospital to the patient"(9). In the Anglo-American concept, well trained paramedics fulfil this task, whereas in some European countries physicians, particularly anaesthesiologists, are responsible for the emergency medical care of these patients(10).

2.1.1 EMS in Scandinavia

In Scandinavia, scattered populations and challenging geographical and climatic conditions necessitate highly advanced medical treatment by qualified prehospital services. Prehospital emergency care in Scandinavia is mainly provided by ground ambulance units staffed by emergency medical technicians, paramedics, and nurses, as well as on-call general practitioners and specialist response units or prehospital critical care teams using aircrafts and rapid response cars(11). Anaesthesiologists as prehospital physicians and their strong participation for all critically ill and injured patients in-hospital is an acknowledged and integrated supplement to the Scandinavian EMS(12). As these services take care of a variety of patient groups, skills are needed not only in procedures, but also in diagnostics, logistics, intensive care, and mass-casualty management(13).

2.1.2 EMS in Finland

In Finland, the national emergency phone number 112 connects the caller to the dispatch centre. Dispatchers use a national criteria-based dispatch system and a tiered EMS response system. Variations exist in the level of prehospital care, due to the independence of each municipality. In larger cities, the fire brigade or hospital districts are the usual EMS providers, whereas private entrepreneurs are most frequently used in rural areas(12). In populated areas, response times for a basic life support (BLS) unit average from 5 to 7 minutes. Advanced life support (ALS) response times vary between 10 to 15, with fire engines acting as first responding units when closest(12). Ground transport to emergency departments (ED) by BLS or ALS units is the most common way of transportation. The prehospital on-site physician does specialist referrals directly from the scene. In areas without prehospital physicians, BLS and ALS units triage and refer patients to hospitals according to local directives.

The BLS personnel mainly consists of practical nurses or fire fighters with 1.5-three years of occupational training. Basic level skills include the use of an automatic external defibrillator (AED), the ability to secure the airway of a lifeless patient, and vascular access. No parenteral drugs are in use(12). The ALS usually employs emergency nurses with four years of training. The ALS units use standard operating procedures (SOPs) and are authorized to give intravenous drugs, provide sedation to facilitate tracheal intubation in unconscious patients, and initiate thrombolytic treatment after consulting with a physician.

EDs are part of the hospital network consisting of 16 central and five university hospitals, which provide immediate neurosurgical care according to national guidelines (the first edition published in 2003, with an update in 2017(14)).

Anaesthesiology services are available in all central and university hospitals. The first-line physicians on-call are usually residents in training, backed up by senior specialists. No formal trauma team or life support certification exists(12).

2.1.3 Prehospital physician-staffed EMS

In 1957, the concept of a physician-staffed prehospital emergency medical team was implemented in the form of a coach, which contained an operating theatre. In 1971 the German HEMS commenced operation with its Christoph rescue helicopters(15).

The first physician-staffed EMS unit in Finland was introduced in the year 1972 in Helsinki. During the 1980's other physician-staffed EMS units were founded and the first physician-staffed HEMS unit was introduced in 1992.

In the consensus article "The top five research priorities in physician-provided pre-hospital critical care"(16) Fevang et al. used the term physician-staffed EMS for all physician-manned prehospital emergency medical teams. The term will be used throughout this thesis when referring to prehospital medical teams that are manned by physicians.

The aim of the physician-staffed EMS is to provide advanced care and interventions beyond the scope of standard EMS to improve the outcome of critically ill or severely injured patients. Physician-staffed EMS is often deployed by helicopter or land-based emergency response vehicle to patients considered likely to require critical care treatment in the prehospital setting. At the time of this thesis, in Finland, six physician-staffed EMS ground units are used in the cities of Helsinki, Pori, Lahti, Seinäjoki, Lappeenranta, and Kouvola and five physician-staffed HEMS units are located in the cities of Turku, Tampere, Kuopio, and Oulu and in the capital Helsinki area. Two more physician-staffed HEMS units are being planned to be operational by the year 2022. The HEMS physicians are mostly anaesthesiologists experienced in prehospital critical emergency medicine.

The controversy surrounding physician-staffed EMS is intriguing, as there seems to be a common consensus regarding the need for physicians treating critically ill patients in the emergency room (ER)(17, 18). Conversely, it could be negligent to deprive patients of the physicians' skill sets and diagnostic capabilities if it is available. Therefore, evidence-based decision-making for the dispatch of EMS and the delivery of advanced interventions is of central importance, balancing the level of safe care appropriate to a patient's need with resource availability and cost benefit. This is a fine balance, demanding reasoning based on evidence and experience, systematically collected and analysed, to increase the chances of making the right decision(19).

2.2 Traumatic brain injury

The term traumatic brain injury includes a wide spectrum of different pathologies and is characterized by a broad heterogeneity in terms of aetiology, mechanism, pathology, and severity. The term head injury is often used synonymously with TBI but may refer to an injury of the skull with no pathological abnormalities in the brain.

Worldwide, TBI is one of the leading causes of death and permanent disability, particularly in young adults(1). In a review of the epidemiology of traumatic brain injuries in Europe, an overall incidence rate of 262 per 100,000 for admitted TBI was derived, and an average mortality rate of 10.5/100,000 was estimated(20).

The epidemiology of TBI has changed over time. A shift toward an older age of patients with TBI has been observed, especially in high-income countries, with falls representing the primary cause of TBI among the elderly, resulting in more contusional injuries. The high incidence of comorbidities and the frequent use of platelet aggregation inhibitors and oral anticoagulants among older patients have a negative influence on outcome following TBI(21). In Europe, TBI accounts for the greatest number of total years lived with disability resulting from trauma and is among the top three causes of injury-related medical costs(22, 23).

TBI is caused by an insult to the brain caused by an external physical force that may produce a diminished or altered state of consciousness, which results in an impairment of cognitive abilities or physical functioning. TBI can be isolated, but it is associated with extracranial injuries in about 35 % of cases(24). Multiple injuries increase the risk of secondary brain damage.

There are three generally acknowledged levels of TBI severity: *Mild* TBI is a trauma to the head that results in a confused state or a loss of consciousness of less than 30 minutes. In this level, the initial Glasgow Coma Scale (GCS) is 13-15, and posttraumatic amnesia lasts less than 24 hours. *Moderate* TBI is a trauma to the head that results in a loss of consciousness from 30 minutes up to 24 hours and an initial GCS of 9-12. Posttraumatic amnesia can last from 24 hours up to seven days. *Severe* TBI is a trauma to the head that results in a loss of consciousness of more than 24 hours, an initial GCS of 3-8, and a posttraumatic amnesia period of more than seven days(14).

The leading causes of TBI in the general population are falls, motor vehicle crashes, blunt impact (e.g., being struck by or against a moving or stationary object), and assaults. Different age groups are affected to varying degrees. Falls account for a large proportion of TBIs among children aged 0–14 years and among adults aged

≥ 65 years. Motor vehicle crashes and assaults are the predominant causes of TBIs in teens and young adults aged 15–34 years(25).

Approximately 10-20 % of all TBIs are moderate or severe in nature, requiring treatment in an intensive care unit (ICU)(26, 27). From this patient group, one in two people die or are left with severe lifelong disabilities, demonstrating the prognosis of TBI(28, 29). Half of those who die from TBI do so within the first two hours of injury. Therefore, EMS personnel are often the primary healthcare providers attending patients with TBI(1). Prehospital assessment and treatment is a critical link in providing appropriate care(30), as the prognosis of patients with severe TBI and low GCS scores depends strongly on the early support of vital functions(3, 4).

As of today, there are no specific diagnostic tests for TBI. The diagnosis of TBI is established based on clinical symptom such as the presence of any documented loss of consciousness and/or amnesia (retrograde or post- traumatic). Additional clinical investigations can be driven by the patient's level of awareness, presence of risk factors, and mechanisms of injury(31). Computer tomography (CT) is the preferred method of assessment on hospital admission to determine structural damage and to detect (developing) intracranial haematomas. Traumatic intracranial lesions occur frequently in severe and moderate injuries, but are also reported in 14 % of patients with a GCS of 14(32).

2.2.1 Primary and secondary brain injury

The pathophysiological mechanism of TBI is traditionally divided into two phases: primary and secondary brain injury. The primary injury is the mechanical damage to the brain parenchyma at the time of impact and is the result of the initial mechanical forces. The primary injury evolves over time, reaching its peak in the succeeding hours and overlapping with the early phases of secondary brain injury. The primary brain injury can include extradural and subdural haematomata, intracerebral contusions, and diffuse axonal injuries.

The secondary brain injury, originally initiated by the primary injury, takes place in the ensuing hours and days and can lead to increased mortality and disability(1). Intracranial and extracranial or systemic insults may complicate the primarily injured brain and result in secondary brain injury(2).

Secondary intracranial brain insults include cerebral oedema, hematomas, hydrocephalus, intracranial hypertension, vasospasm, metabolic derangement, infections, and seizures(33, 34). Secondary systemic brain insults are mainly ischemic in nature. As cerebral oxygen delivery is partly determined by arterial oxygen content and partly by cerebral blood flow (CBF), it is affected by cerebral autoregulation. When the autoregulation is impaired, a correlation between mean arterial pressure (MAP) and CBF exists, making the brain susceptible to ischemia or hyperemia(35, 36).

The management of severe TBI focuses on the prevention of a secondary ischemic brain injury by optimizing the balance between cerebral oxygen delivery and utilization(3, 6). Therefore, the treatment focuses on inhibiting the progression of the primary brain injury and preventing and reversing a secondary brain injury(2, 6). In particular, prehospital prevention of hypoxia by adequate respiratory management, including a secured airway, normoventilation, and the prevention of aspiration, is strongly associated with improved outcomes(37-40).

2.2.2 TBI patient prognosis

The Glasgow Outcome Score (GOS) is a scale that applies to patients with brain damage, allowing the objective assessment of their recovery. The first description was in 1975 by Jennett and Bond(41). In 1981, Jennett and colleagues expanded the five-point GOS into an eight-point scale extended GOS (GOS-E) by dividing each of the moderate, severe disability, and good recovery categories into two: better and worse(42).

The original GOS and GOS-E are recommended by several national bodies and are the most highly cited outcome measures in studies on brain injury(43). The benefits of GOS are that it is freely available, simple to use, and requires little training. It has also been validated and proven reliable with adult and paediatric versions available.

The original GOS scale consists of five categories (Table 1), each of which is descriptive; the three most positive categories are related to social function and return to work.

Table 1. The GOS categories(41)

1. Death	Death
2. Vegetative state	Severe damage with prolonged state of unresponsiveness and a lack of higher mental functions
3. Severe disability	Severe injury with permanent need for help with daily living
4. Moderate disability	No need for assistance in everyday life, employment is possible but may require special equipment
5. Good recovery	Light damage with minor neurological and psychological deficits

The outcome after a head injury is generally assessed at six months after the injury. About 90 % of the recovery occurs within this time period(42). Survivors of severe TBI have a low life expectancy, dying over three times faster than the general population(44). Most survivors are left with severe lifelong disabilities(28, 45, 46). Furthermore, survivors face prolonged care and rehabilitation, and have consequent long-term physical, cognitive, and psychological disorders that affect their independence, relationships, and employment(46). In 2007, a conservative estimate of lifetime costs per case of severe TBI was US$ 396,331, with costs for disability and lost productivity ($ 330,827) outweighing those for medical care and rehabilitation ($ 65,504)(47).

A large meta-analysis has shown decreasing mortality rates in patients with severe TBI by almost 50 % over the last 150 years. It also showed mortality rates were steady from 1930 until 1970, at which point mortality decreased at a rate of 9 % per decade until 1990. Mortality has remained stable at approximately 35 % ever since suggesting no advances in patient outcomes over the last quarter-century(48). On the other hand, studies after 1990 have also reported improvements in TBI patient outcomes as a result of an advancement in TBI care guideline development(49, 50) and active intensive care(51-54), for example.

2.3 TBI prognostic factors

Large registry studies have revealed that outcomes in TBI profoundly rely on demographic and trauma-related factors, such as age, motor score, pupillary reactivity, CT classification, and secondary factors, such as hypoxia and arterial hypotension(29, 55-57).

This thesis aims to more specifically evaluate the relationship between the role of EMS physicians and prehospital treatable secondary brain injury risk factors, including prehospital hypoxic or hypotensive events, with outcomes in patients with severe TBI. The evaluation is performed in the context of the prehospital environment with predictors that are of value in the prehospital treatment phase(58).

2.3.1 The effect of patient demographics on TBI prognosis

Age is known to have prognostic value following TBI, and older patients have been reported to have increased mortality and worse functional outcomes compared to younger patients(59-64). The full extent of the impact of age has yet to be examined(64). In moderate to severe isolated head injuries, it has been noted that the patients admitted for head trauma are distributed by age groups with two typical peaks in the 21–30 and 71–80 age groups(59).

Age has an effect on mortality independent of other factors(63). This might be related to the properties of the aging brain and its ability to heal, the type of brain injury, or because aging affects the physiologic status and creates a more destructive injury(63, 65). Scalea et al.(66) have suggested elderly trauma patients have diminished cardiac hemodynamics and require aggressive monitoring and resuscitation with more pre-existing comorbidities that could alter the physiologic response to injury and result in more complications. It has also been suggested that the elderly mortality rate from head injury is higher because less aggressive therapy is initiated in the earlier stages of treatment, but no clear evidence of this has been shown(59, 63). As noted earlier, the high incidence of comorbidities and the frequent use of platelet aggregation inhibitors and oral anticoagulants among older patients have a negative influence on outcomes following TBI(21, 67).

A clear correlation has also been found between age and the mechanism of the injury. Falls are thus becoming a more and more important cause of TBI, mainly in the high-income regions of Europe. Falls are most common in two age groups: the elderly and children. In contrast, road traffic accidents (RTAs) are the most frequent cause in young adults(20), and their role as a cause of severe TBI is dominant. RTA deaths are projected to increase from 1.2 million in 2002 to 2.1 million in 2030, primarily due to increased motor vehicle fatalities associated with economic growth in low- and middle-income countries(68).

Even though TBI is more common in young men(69, 70), the gender difference is only seen from puberty until middle age. During a large part of the life span, the TBI rates are roughly equal between the sexes, as there are no gender differences in the incidence of children sustaining TBI(71). When considering adults, the incidence of TBI appears to be approximately the same in men and women aged 45 to 75 years. After age 75 , there is a slightly higher incidence of mild head injury in women, mostly due to falls(70). It has been reported that females experience worse overall outcomes after TBI compared to male survivors(72), although this remains controversial, as the contradictory has also been reported(73).

2.3.2 GCS

The Glasgow Coma Scale has been widely adopted in clinical practice and health care research as an instrument for assessing the (depressed) level of consciousness(74). The GCS was developed by Teasdale and Jennett in 1974(75) and is widely used in the prehospital setting. The acronym GCS can refer to either the Glasgow Coma Scale (individual components) or the Glasgow Coma Score (total sum of components).

Over time, the sum score has been included in various clinical stratification and outcome prediction scores, such as Acute Physiology and Chronic Health Evaluation (APACHE) II, Revised Trauma Score (RTS), and Trauma and Injury Severity Score (TRISS), and has been adopted in several guidelines, such as the National Trauma Triage Protocol and severe TBI guidelines.

The GCS consists of three components: eye response, verbal response, and motor response, which are added together for a score from 3 to 15. The GCS is traditionally used to classify TBI into mild (GCS 13-15), moderate (GCS 9-12), and severe (GCS 3-8)(76). Individual patients are best described by the three components of the coma scale; whereas the derived total coma score should be used to characterize groups(74).

The prognostic value of the sum score has been extensively studied in patients with TBI. Lower sum scores have been associated with poorer outcomes, and an approximately linear relation between mortality and sum score is reported in patients with TBI(74). The relationship between prehospital GCS and mortality and neurological outcomes in TBI has been found to be a significant and reliable indicator of the severity of the injury(30, 77-80). Mortality increases and neurologic outcomes worsen in patients with a GCS score below 8. In particular, a GCS score of 3 at presentation has been associated with a significantly poor outcome(81-83). However, mortality rates may differ for patients with different combinations of the three component scores despite similar sum scores(84, 85). It is possible for patients to have the same total GCS score but significantly different risks of mortality due to differences in the GCS profile making up that score(85).

2.3.3 Pupillary size and light reactivity

Poor reactivity or pupil dilation is thought to be a result of third cranial nerve compression and subsequent brain stem compromise. In general, this process starts asymmetrically leading to a unilateral pupil dilatation that may evolve to bilateral mydriasis and, if not quickly reversed, evolves to brain death. It has also been suggested that poor reactivity or dilated pupils may be a result of reduced blood flow to the brain stem when compromised autoregulation could vary according to changes in blood pressure.

Pupillary size and light reactivity are vital to the neurologic assessment of patients with a history of head trauma. An acute dilation of the pupil and unresponsiveness to light is considered a neurological emergency and is strongly associated with a poor prognosis(86). In patients with severe TBI, the mortality has been shown to increase in mean three and 20 times, respectively, in patients admitted with unilateral or bilateral mydriasis in comparison to those with isochoric pupils(87).

Pupillary function may be an indicator of brain injury after trauma, but it is not a specific indicator of injury severity or involved anatomy(1). Asymmetry is defined as > 1 mm difference in diameter and fixed pupil as < 1 mm response to bright light(1). It is recommended that in-hospital post-stabilization values be used for clinical trial design and prognosis(86).

2.3.4 Hypotension

The three main factors determining cerebral oxygenation are CBF, arterial oxygen content, and cerebral metabolic rate of oxygen consumption. The cerebral perfusion pressure (CPP) is the difference between the mean arterial blood pressure (MAP) and the intracranial pressure (ICP). CPP is the most frequently used surrogate for CBF measurements. It represents the vascular pressure gradient across the cerebral vascular bed. CPP is easily performed, provides a continuous measurement, and forms part of the management guidelines of the Brain Trauma Foundation. However, the optimal CPP threshold continues to be controversial(88).

Autoregulation is a term used for a process maintaining a relatively stable CBF. It can be defined as the ability of arteries to vasodilate or vasoconstrict in response to changing perfusion pressure. Autoregulation can become impaired or abolished by a variety of insults including trauma, hypoxemia, hypercapnia, and large-dose volatile anesthetics(89). TBI can lead to a situation where CBF becomes dependent on blood pressure.

The level of systolic blood pressure (SBP) has long been felt to play a critical role in the secondary injury cascade after severe TBI(6). Hypotension can result in reduced cerebral perfusion and neuronal ischaemia. Additionally, hypotension has been shown to correlate with diffuse brain swelling(90). There are several underlying pathophysiologic mechanisms. If autoregulation remains intact, a drop in SBP triggers an autoregulatory vasodilation to maintain adequate brain perfusion. This results in an increased cerebral blood volume, which in turn elevates intracranial pressure(6). If autoregulation is not intact, there is a dependency on SBP to prevent cerebral ischemia, which has been ascribed to be the most important secondary insult(91).

The TBI guidelines recommend a minimum systolic pressure of 90 mmHg in adults with severe TBI(1). This target is based on studies showing higher mortality with a SBP of less than 90 mmHg (3, 77, 92-95). TBI studies typically incorporate SBP as a binary variable with a cut-off value of 90 mmHg, although the defining level of hypotension in TBI is unclear. At the time of this thesis, studies have been done suggesting SBP values higher than 90 mmHg are most likely beneficial for patients with isolated severe TBI(95-100). MAP may be of greater relevance than SBP in TBI due to its direct influence on CPP(88).

2.3.5 Hypoxia and airway

As early as 1978, Miller suggested brain ischemia after an injury could be exacerbated by secondary insults, and care for the patient with head injuries should start at the roadside(101). Since then, it has been concluded that hypoxemia is a strong predictor of the outcome in TBI, and the negative effect of hypoxemia on the outcome has been demonstrated in several studies(3, 4, 56, 92, 102).

Early definitive airway control has become an established principle in the management and resuscitation of critically injured patients. Particularly in a patient with a head injury, where hypoxemia and hypercapnia can worsen the brain injury, this practice in considered standard(103).

The current prehospital guidelines recommend avoiding and correcting hypoxemia (oxygen saturation $SpO_2 < 90$ %) immediately upon identification using supplemental oxygen and varying combinations of bag mask ventilation, endotracheal intubation, and other airway adjuncts(1).

Advanced airway management is defined in the current guidelines as the use of a device (endotracheal tube, laryngeal mask airway, or oesophageal tracheal tube), not including oropharyngeal and nasopharyngeal airways, to ensure a patent airway(1).

When considering the possible benefits of the prehospital endotracheal intubation of TBI patients, the literature is inconclusive(104). Some studies indicate benefits in survival, while others show increased mortality(37, 79, 105). Desaturations (SpO_2 < 70 %) during intubation or any oxygen desaturation (SpO_2 < 90 %) has been associated with higher mortality(106). Most studies are retrospective and study paramedics performing endotracheal intubation with a minimal use of sedative agents and muscle relaxants.

A recent systematic review addressed the effect of the EMS providers' experience on prehospital intubation (PHI). The review concluded that PHI by healthcare professionals with limited experience is associated with increased mortality and suggested such providers should not routinely perform PHI in severe TBI patients(107). According to current knowledge, prehospital endotracheal intubation by EMS physicians is a safe procedure with low complication and high success rates(108-117).

2.3.6 Ventilation

According to the TBI guidelines, normal ventilation is the goal for severe TBI patients(103). Under normal conditions, $PaCO_2$ is the most powerful determinant of CBF. Therefore, low $PaCO_2$ results in low CBF and may result in cerebral ischemia, while high $PaCO_2$ levels can result in cerebral hyperaemia and high ICP(103).

Some studies have focused on the impact of prehospital ventilation on the TBI outcome. According to these studies, hyper- and hypoventilation are associated with worse outcomes(40, 106, 118-122). However, hyperventilation may be a life-saving intervention in the setting of acute brainstem herniation(123, 124). Apart from this specific indication, there is a consensus that preclinical hypoventilation as well as hyperventilation should be avoided in severe TBI(5, 125).

2.3.7 Prehospital time frames

One of the most well-known principles in prehospital medicine is the golden hour of trauma(126), even though the evidence for the golden hour and timing of craniotomies for head injuries on patient outcomes is limited(127-129). The prehospital time frames can be divided into activation time (AT), response time (RT), on-scene time (OST), transport time (TT), and total prehospital time (TPT)(130).

The literature is inconclusive about the effect of prehospital mission times on the outcomes of severe TBI patients(58, 129, 131-134). This is most likely associated with different prehospital treatment strategies (such as scoop-and-run and stay-and-treat) and interventions, such as the airway management performed on-scene, which influence the OST and could have an impact on the outcomes of the TBI patients. It has also been suggested that an indirect transfer of TBI patients is associated with a 50 % increase in mortality, and a direct transfer to a trauma centre is indicated even if this centre may not be the closest hospital(135).

2.3.8 Other potential prehospital interventions

Despite the potential benefits of early intervention, few prehospital treatment options have proved effective(46). Lifting the upper body to a 15-30° angle with the head in a neutral position is a widely approved treatment, although the scientific evidence is scarce(14).

There are no trials comparing the efficacy of different anaesthetics for prehospital rapid sequence intubation (RSI) in patients with severe TBI. A systematic review of sedation for critically ill adults with severe TBI found no convincing evidence that one sedative agent is more efficacious than another for the improvement of patient-centred outcomes, ICP, or CPP(136). Anaesthetics with vasodilatory features may induce unwanted hypotension, resulting in secondary brain injury(5).

Tranexamic acid is an anti-fibrinolytic drug that could reduce the risk of mortality and disability from TBI (46, 137). In the CRASH-2 trial(138), tranexamic acid reduced mortality in trauma patients, but the results from a sub-study of TBI patients of CRASH-2 were inconclusive(139). This was further studied in the CRASH-3 trial with the conclusion that tranexamic acid is safe in patients with TBI, and treatment within three hours reduces head injury-related deaths in mild-to-moderate TBI, but not in patients with severe TBI(140).

In theory, hypertonic solutions influence ICP by producing an osmotic gradient between the intravascular and the intracellular/interstitial compartments. Although it has been suggested that prehospital resuscitation with hypertonic saline is associated with a reduction in the serum levels of commonly assessed biomarkers of brain injury(141), hypertonic solutions have not proven to be more effective than isotonic saline(142-144). Studies also suggest hypertonic saline solutions are slightly more effective than mannitol at reducing ICP in patients with established intracranial hypertension(145-148), but high-quality clinical trials have not reported improved survival or neurological outcomes(149).

Although mild therapeutic hypothermia (MTH) has theoretical benefits, including a reduction or delay in metabolic consumption during the stress of a central nervous system (CNS) injury, no effect on the outcome has been shown(150-153). A recent study found no differences in the rates of poor neurological outcomes or mortality among patients with severe TBI who received prolonged (≥ 72 h) MTH (32–34°C), slow rewarming and neurological intensive care compared to those who received only strict fever control (35.5–37°C)(154).

Hyperoxemia has been proposed to improve cerebral oxygenation and outcomes in TBI patients(5). While mild hyperoxemia has been suggested to have beneficial effects in TBI, extreme hyperoxemia has been associated with increased mortality and decreased positive outcomes among TBI patients(155). Targeting hyperoxemia seems to be a safe approach when trying to maintain adequate brain oxygenation(156).

In the CRASH trial, there was no evidence of the effect of corticosteroids in adults with severe TBI as the risk of death was higher in the treatment group than in the control group(157). Furthermore, a review did not find evidence that progesterone could reduce mortality or disability in patients with TBI(158).

3 AIMS OF THE STUDY

The aim of this thesis is to evaluate the effect of a physician-staffed EMS in the treatment of prehospital patients with a focus on prehospital airway management and TBI. The hypothesis was that the implementation of a physician-staffed EMS would have a positive effect on patient outcomes.

The specific aims were:

1. Evaluate the long-term outcomes of critically ill or severely injured patients treated by an EMS physician in the prehospital setting (I).

2. Evaluate the impact of EMS physicians treating prehospital severe TBI patients in differently structured EMS systems (II-IV).

4 MATERIAL AND METHODS

4.1 Study setting

Finland covers an area of 338,000 km^2 with a population of 5.5 million. Half of the population lives in the south, whereas the middle and especially the northern parts of the country are mainly rural. Organizing EMS system is the responsibility of 20 hospital districts. In larger cities, the fire brigade is the usual EMS provider, whereas private entrepreneurs are most frequently used in rural areas. Generally, the EMS system in general is three-tiered: basic life support (BLS), advanced life support (ALS), and physician-staffed units. Rescue departments and voluntary service fire engines can also be used as first responders.

4.1.1 The Pirkanmaa paramedic-staffed EMS system

The Pirkanmaa Hospital District is situated in South-Western Finland. There are approximately 200,000 inhabitants in the city of Tampere and another 250,000 inhabitants in the surrounding communities. Until the year 2011, there were no dedicated EMS medical directors, and prehospital crews consulted on-call hospital physicians and local general practitioners for treatment guidelines. Physician-staffed prehospital units and online medical supervision were not available. Paramedic-staffed EMS units provided prehospital care in this region. During the study period, patients with a decreased level of consciousness were routinely administered oxygen according to national guidelines. Neuromuscular blocking agents were not available in the prehospital service, and prehospital advanced airway management was performed using sedatives and opioids, if at all.

4.1.2 The Pirkanmaa physician-staffed EMS system

A physician-staffed HEMS was introduced into the EMS in the autumn of 2011, covering all 22 municipalities in the region. The HEMS is dispatched on primary missions together with basic or advanced life support EMS units. The role of the helicopter is primarily to transport the physician to the scene. Subsequently patient transport is usually carried out by EMS ground vehicles with the physician escorting the patient unless significant time gain is anticipated. In these selected cases and when logistically beneficial, transportation by the helicopter unit is used. The physicians are anaesthesiologists experienced in prehospital critical emergency medicine who conduct advanced airway management according to the HEMS unit TBI standard operation procedure (SOP).

General anaesthesia complying with the principles of neuroanaesthesia, including hypnotics, opioids, and neuromuscular blocking agents, is routinely used for RSI. Capnography-assisted controlled ventilation and invasive haemodynamic monitoring with arterial blood gas sampling are also routinely used. If necessary, noradrenaline-infusion and hypertonic saline are administered according to the unit's TBI SOP and national guidelines. One university hospital provides tertiary care in the region.

4.1.3 The Helsinki and Uusimaa area physician-staffed EMS system

The Helsinki and Uusimaa Hospital District is situated in the southern part of Finland, and a total of 1.3 million people inhabit the capital area. The hospital district's EMS system is three-tiered with two physician-staffed units: a physician-staffed mobile intensive care unit serving the city of Helsinki and a HEMS unit serving the rest of the region. The physician-staffed units provide the third tier and operate as described above. As in the Pirkanmaa hospital district, one university hospital operates as the tertiary referral centre, providing standardized immediate neurosurgical care according to national guidelines.

4.2 Data collection

To evaluate the long-term outcomes of critical patients treated by an EMS physician in the prehospital setting, data of 483 critically ill or severely injured patients treated by the Helsinki region HEMS between 2007-2011 were analysed (I). The study patients were gathered from the HEMS database, and the need for prehospital advanced airway management was used as an indicator to identify critical prehospital patients.

To evaluate the role of EMS physicians' involvement, the prehospital treatment and outcomes of patients with severe TBI from 2005-2010 and 2012-2015 in two study locations (the Helsinki and Uusimaa region and Pirkanmaa region, Finland) were determined for this thesis (II-IV). The Helsinki and Uusimaa area represents a 10-year patient flow in a physician-staffed EMS system. The Pirkanmaa patient cohort is divided into two sections: 2005-2010 with no prehospital physician service and 2011-2015 after the implementation of a physician-staffed EMS unit. The data covering 2011 were excluded, as a physician-staffed HEMS was implemented in the Pirkanmaa Hospital District that year and significantly impacted the local EMS. Included patients were identified based on the ICD-10 discharge diagnosis for TBI (S06.2-S06.6, S06.8) retrieved from their records. Inclusion criteria for the studies were as follows: severe isolated TBI presenting with unconsciousness defined as a GCS score ≤ 8 occurring either on-scene, during transportation, or verified by an on-call neurosurgeon on admission to the hospital. Patients with concomitant multiple injuries with the need for emergency surgical interventions (other than neurosurgery) were excluded, as were patients transferred from other hospitals (inter-hospital or, in other words, secondary transfers).

Age, gender, prehospital time frames, mechanism of the injury, GCS score, vital signs, and treatment were reviewed on-scene and on arrival at the ED when appropriate for the specific study in question. Patients' neurological statuses six months or one year after their incident was determined from hospital records and assessed with a simplified three-category six-month GOS. A GOS of 1 denoted death within six months, GOS 2-3 denoted a poor neurological outcome (need for assistance in activities of daily living), and GOS 4-5 denoted good neurological recovery (independent life). Mortality data were obtained from the national statistical authority, Statistics Finland.

For studies II-IV, an overview of the patients is presented in Table 2, where the cohorts have been grouped A-D in relation to the EMS system to visualize comparisons. The number of patients in these groups are based on publication IV and slightly differ between the original publications due to the differences in the used follow-up periods and the availability of mortality and neurological outcome data in each publication. For more details, please refer to the flowcharts in the original publications attached to this thesis.

Table 2. Overview of the study patients

Group	Year	EMS	Location	n
A	2005-2010	paramedic	PSHP	181
B	2005-2010	physician	HUS	270
C	2012-2015	physician	PSHP	85
D	2012-2015	physician	HUS	115

PSHP = Pirkanmaa hospital district
HUS = Helsinki and Uusimaa hospital district

Groups A and B were compared in paramedic- versus physician-staffed EMS settings (II). Groups A and C were compared in a before-after setting regarding the implementation of a physician-staffed HEMS (III). To predict survival and good neurological outcomes for all studied patients, group D, previously unused data (representing 18 % of the total information), was added to groups A-C. The data was further analysed using a binary logistic regression analysis (IV). The evaluation was performed in the context of the prehospital environment with predictors that have been shown to have prognostic value in the prehospital treatment phase.

4.3 Statistical methods

Results are expressed as medians and ranges or percentages, while categorial variables were compared using the chi-square or Fisher's exact test. The odds ratios and 95 % confidence intervals were calculated using univariate and multivariable binary logistic regression to identify predictors of good neurological outcomes and one-year mortality (II, III, and IV). Comparisons between groups were performed using the log-rank test (II, III), and variables of the univariate analysis with $p < 0.05$ were added to the multivariable analysis (III). Kaplan-Meier survival curves illustrate the survival in different prehospital patient groups (I), the one-year survival rate in the comparison between paramedic- and physician-staffed EMSs (II), and the difference in the six-month survival rate after the implementation of physician-staffed EMS (III).

In study IV, a binary logistic regression analysis was used to predict survival and good neurological outcomes. The following known conventional prognostic variables for TBI were available in the prehospital setting: age, on-scene GCS, hypoxia, and hypotension. Based on the hypothesis that the treatment provided by on-scene EMS physicians would be beneficial, EMS physicians were added to the analysis as a potential predictive factor for prognosis.

The data were analysed using IBM SPSS Statistics for Windows (Version 21.0; IBM Corp., NY, USA), released in 2012. For all studies, statistical significance was considered at a value of less than 0.05.

4.4 Ethical considerations

The protocol for study I was approved by the Coordinating Research Director of the Helsinki University Hospital. As the study was observational and analysed routinely collected data, the approval from the Ethics Committee was not considered mandatory at the Helsinki University Hospital.

The protocols for studies II-IV were reviewed by the Regional Ethics Committee of the Pirkanmaa Hospital District with permissions to conduct the studies obtained from the Research Directors of Tampere (II-IV) and Helsinki University Hospitals (II, IV).

All studies were registered in ClinicalTrials.gov: NCT02307123 (I), NCT02307123 (II), NCT02659046 (III, IV).

5 RESULTS

An overview of the study designs and main results of the studies included in this thesis are presented in Table 3.

Table 3. Overview of study designs and main results

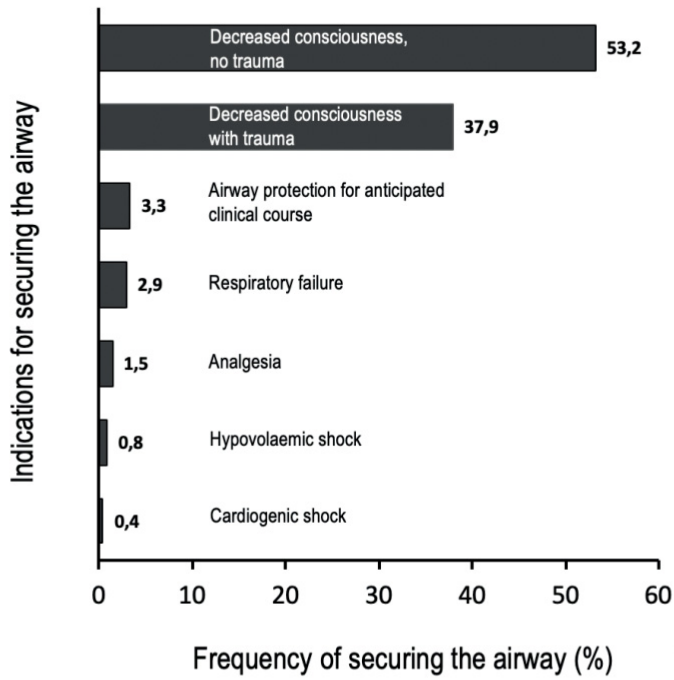
	Study I	**Study II**	**Study III**	**Study IV**
Study question	Long-term outcomes of critical prehospital patients treated by EMS physicians	Outcomes of TBI patients in two regions with differently structured EMS systems	The effect of introducing a physician-staffed HEMS in the treatment of severe TBI patients in a before-after setting	Binary logistic regression analysis and evaluation of the effect of EMS physicians on TBI patients
Number of patients	483	451	266	651
Years	2007-2011	2005-2010	2005-2010 2012-2015	2005-2010 2012-2015
Main outcome	1-year mortality and neurological outcome	1-year mortality and neurological outcome	6-month mortality and neurological outcome	6-month mortality and neurological outcome
Main result	35% mortality, good recovery: 85% of the survivors	Lower mortality in physician- (42%) treated compared to paramedic-treated (57%) TBI patients (p=0.001)	Improved neurological outcomes after (42% vs. 28%) the implementation of physician-staffed HEMS (p=0.022)	An on-scene EMS physician treating severe TBI patients was associated with lower mortality (OR 0.53, p=0.005) and better neurological outcomes (OR 1.75, p=0.020)

Good recovery = Light damage with minor neurological and psychological deficits(41)

5.1 Long-term outcomes of critical patients treated by EMS physicians

Advanced airway management was used as an indicator of the severity of the patients' conditions in 483 critically ill or severely injured patients (excluding cardiac arrest) who were treated in the prehospital setting by the Helsinki area HEMS between 2007-2011 (I). The main indication for PHI in the study population was a decreased level of consciousness without trauma or due to trauma. Other indications were a minority, as they covered less than 10 % of the cases (Figure 1). The main prehospital diagnoses were trauma with isolated or concomitant head injury (32.9 %) and suspected spontaneous intracranial pathology (21.7 %). Males were most often suspected to have a decreased level of consciousness due to an isolated or concomitant head injury (36.2 %), whereas in females, the most frequent prehospital diagnosis was spontaneous intracranial pathology (28.5 %).

Figure 1. Indications for PHI in study I



The patients' one-year mortality (GOS 1) was 35 %. The probability of death increased with age (OR 1.05; 95% confidence interval 1.04-1.06). Of the patients who died, 43 % died within the first 24 hours, and 68 % within a week and 82 % within 30 days after the incident. Good neurological recovery (GOS 4-5; i.e., the ability to live an independent life) was found in 55 % of the patients. Most of the patients in the younger age groups (below 60 years of age) and 85 % of the survivors recovered neurologically well.

5.2 The impact of EMS physicians treating TBI patients

5.2.1 Patient characteristics

The TBI study populations are shown in Table 4.

Table 4. Baseline characteristics

Study	Paramedic vs. physician EMS II	Introduction of physician into paramedic EMS III	Effect of on-scene physicians on outcomes IV
No. patients	451 (181+270)	266 (181+85)	651 (181+270+85+115)
Age (y, median, range	54 (6-89) / 50 (0-90)	54 (6-89) / 53 (4-92)	50 (0-92)
Gender (male, %)	70 % / 74 %	70 % / 68 %	74 %
Primary GCS (median)	5 / 4	5 / 5	5
Airway secured (%)	16 % / 98 %	16 % / 95 %	74 %

5.2.2 Comparison of outcomes in paramedic- versus physician-staffed EMS

The characteristics and neurological outcomes of 451 TBI patients treated in two differently structured EMSs during a six-year period were studied (II). The paramedic-treated cohort included 181 TBI patients, and the physician-treated cohort included 270 patients. The baseline characteristics of the patients were similar (Table 4). The response time of the first EMS unit on-scene did not differ between the groups. However, the total mission times were shorter in the paramedic-treated group with a median time of 54 (range 18–180) minutes compared to the physician-treated group with 72 (range 23–191) minutes ($p < 0.001$).

Hypotension was present on-scene in 4 % of the patients treated by paramedic-staffed EMS, and hypoxia was documented in 19 %. The corresponding figures in the patients treated by physician-staffed EMS were 3 % ($p = 0.44$) and 15 %, ($p =$

0.31), respectively. Advanced airway management was performed in 16 % of the patients in the paramedic EMS group and in 98 % of the patients in the physician EMS group ($p < 0.001$). When considering the treatable reasons for a secondary brain injury at the time of arrival to the ED, hypotension was recorded in 4 % of the patients in both study groups, but the patients in the paramedic EMS group were more often hypoxic (10 % vs. 1 %, OR 10.05 CI 2.91–34.67, $p < 0.001$).

One-year mortality was higher in the paramedic EMS group: 57 % vs. 42 % (OR 1.86 CI 1.27-2.71, $p = 0.001$). A good neurological outcome was less common in patients treated by paramedics with 32 %, as 38 % (OR 0.74 CI 0.5-1.11, $p = 0.14$) of the patients treated by physicians had a good neurological recovery (GOS 4–5) with independent life one year after the event. In the multivariable analysis after the patients were adjusted by age, the EMS system remained as a significant risk factor for mortality (OR 1.69 CI 1.11-2.58, $p = 0.015$).

5.2.3 Introducing HEMS to a paramedic EMS system

The six-month outcomes of 181 TBI patients who were treated during the paramedic EMS period in the Pirkanmaa region were compared in a before-after setting with the outcomes of 85 TBI patients after the introduction of a physician-staffed HEMS unit (III). The baseline characteristics and the first recorded vital signs of the two cohorts were similar.

Good neurological outcomes were more frequent after the introduction of the HEMS; 42 % of the HEMS-managed patients and 28 % ($p = 0.022$) of the patients managed by the paramedic-EMS had a good neurological recovery (GOS 4-5). There was a tendency towards a higher survival rate (53 % vs. 43 %, log rank $p = 0.066$) in the HEMS group during the six-month follow-up period. When two patients were excluded from the analysis because the attending HEMS physician made a prehospital decision to withhold treatment, a Kaplan-Meier analysis resulted in a higher survival rate ($p = 0.045$) of the HEMS-treated patients.

The airway was secured more frequently in the HEMS group ($p < 0.001$). On arrival at the ED, patients in the HEMS group were less often hypoxic ($p = 0.024$). In the univariate analysis, HEMS, a lower age, and a secured airway were associated with good neurological outcomes.

5.2.4 Mortality and neurological outcomes

Table 5. Mortality and neurological outcomes

Study	Paramedic vs. physician EMS II			Introduction of physician into paramedic EMS III			Effect of on-scene physicians on outcomes IV	
Outcome	one-year			six-months			EMS physician effect	
	paramedic (%) n = 181	physician (%) n = 270	p-value	paramedic (%) n = 181	physician (%) n = 85	p-value	physician effect n = 651	p-value
Mortality	57	42	0.001	53	43	0.066	decreased	0.005
Good	32	38	0.14	28	42	0.022	increased	0.02

Good recovery = Light damage with minor neurological and psychological defects(41)

In general, the results of study I showed a good overall neurological recovery from a critically illness or severe injury. In this thesis, with a focus on TBI patients, the results point to an outcome benefit from EMS physicians treating severe TBI. When two regions with differently structured EMS systems were compared, the mortality was lower with EMS physicians present on-scene, as the EMS system without EMS physicians remained a risk factor for mortality ($p = 0.015$) in the multivariable analysis after the patients were adjusted by age (II).

The results also show better neurological outcomes in patients treated by EMS physicians and in the univariate analysis, EMS physicians ($p = 0.022$), a lower age ($p < 0.001$), and a secured airway ($p = 0.017$) were associated with good neurological outcomes (III).

Based on these findings, the gathered TBI patient data were further analysed with a binary logistic regression analysis (IV). The mortality data for 651 patients and the neurological outcome data for 634 patients were available for analysis. Hypoxia was present on-scene in 16 % of the patients, and hypotension was documented in 3 %. The incidence of hypoxia (4 %) was lower, and hypotension (4 %) was slightly higher on arrival at the ED. A physician was present on-scene in 72 % of the cases, and advanced airway management was performed in 74 % of the patients. The airway of 97 % of the patients was secured in the prehospital setting when an on-scene EMS physician was present.

In the univariate analysis, an increasing age, a lower on-scene GCS, and prehospital treatment without the presence of an EMS physician were factors associated with higher mortality. In the multivariable analysis, these variables, with the addition of hypotension, remained significant factors for mortality.

Factors associated with good neurological outcomes in the univariate analysis were a lower age, a higher on-scene GCS, and the presence of an on-scene EMS physician. In the multivariable analysis, all these factors remained significant for a good outcome, while hypotension was associated with a poor outcome.

The significant results of the logistic regression analysis of studies II, III, and IV are presented with more detail in Table 6.

Table 6. Logistic regression analysis of studies II, III and IV

		Univariate			Multivariable		
		OR	95% CI	p-value	OR	95% CI	p-value
Mortality							
Study II	EMS physician	1					
	Not present	1.60	1.22-2.08	0.001	1.69	1.11-2.58	0.015
Study IV	EMS physician	1					
	Not Present	2.03	1.44-2.88	< 0.001	1.89	1.20-2.94	0.005
Good recovery							
Study III	EMS physician	1.87	1.09-3.21	0.022	2.46	0.89-6.84	0.083
	Not present	1					
Study IV	EMS physician	1.97	1.36-2.86	< 0.001	1.75	1.09-2.80	0.002
	Not present	1					

Good recovery = Light damage with minor neurological and psychological deficits(41)

6 DISCUSSION

6.1 Main findings

When PHI was used as a definition of a critical EMS patient it was found that more than half of these seriously ill or injured patients had a favourable long-term neurological recovery. However, the long-term mortality was close to one-third of the population, which most likely reflects the critical conditions leading to PHI.

Focusing on the main prehospital diagnosis of study I, trauma with isolated or concomitant head injury, a comparison between two differently structured EMS systems revealed that physician-staffed EMS systems had an impact on the one-year mortality of TBI patients. Moreover, after the introduction of a physician-staffed HEMS unit into a paramedic EMS system, the beneficial impact was further confirmed, as in a six-month follow-up period, good neurological outcomes were more frequent in the physician-staffed EMS. Furthermore, in the binary logistic regression analysis, the presence of EMS physicians was associated with lower mortality and favourable neurological outcomes.

6.2 EMS system evaluation

Like every part of the health care system, a specialized prehospital EMS should aim to optimize its use of resources, and critically review as well as continuously assess the quality of its established practices. EMS systems and prehospital care are difficult to evaluate. Accordingly, the true efficacy and value of such systems are difficult to determine(7). It has been stated: "There is more solid scientific evidence about topics such as herbal medicine, acupuncture, hives, and constipation than there is about the entire practice of EMS(159)." Reliable answers to questions about the cost benefit are difficult to find, mainly due to methodological problems, as is often the case with emergency medical care. Randomized controlled trials (RCTs) may not be feasible because of ethical and informed-consent issues; a large-scale RCT looking at physician versus non-physician EMS systems would be very challenging to perform(13).

Although HEMS is a part of the prehospital trauma system in many countries, this service and the possible impact it has on the outcomes of traumatically injured patients also remains a subject of debate. Studies have been performed to evaluate the effect of HEMS on the outcomes of trauma patients with contradictory results(160-164). It has been questioned that whether it is the H or the EMS in HEMS that has an impact on trauma patient mortality(165). The study concluded that the debate whether the role and structure of HEMS in a modern trauma service is beneficial is likely to continue.

6.3 Long-term outcomes of critical patients treated by EMS physicians

General long-term follow-up studies on prehospital patients are few, and the question of how long the follow-up period should be has not been answered. Studies with prehospital trauma patients(116, 132, 133) with a special focus on TBI(58, 132, 166) have been previously conducted, but the mortality rates have been reported either as the discharge(116, 132) or 30-day mortality(133).

The creators of GOS concluded in their studies that it was exceptional for a TBI patient who was severely disabled at three months after the injury to ever reach the category of good recovery(42). Their studies also showed that, in cases of TBI, most patients had reached their final outcome category within six months of the injury, and very few changed categories after a year.

Based on the findings of study I, the prehospital diagnosis is likely the determinant factor influencing the long-term survival of a critical prehospital patient. The study population was divided into subgroups: while the one-year mortality of patients suffering intoxications and convulsions was less than 20 %, over half of the patients with intracranial pathology died. In all subgroups, the initial mortality rate was high, and over 80 % of all deaths occurred in the month following the incident. Thus, the results suggest that the previous studies reporting 30-day mortality will give a reasonable estimate of the long-term survival of patients.

After the incident, 85 % of the long-term survivors recovered and were back to an independent life. A notably high mortality rate was observed, but that could reflect the critical condition of the treated patients, and it highlights the positive outcomes of the survivors even more.

6.4 The impact of EMS physicians treating TBI patients

The aim of the physician-staffed EMS is to provide advanced care and interventions beyond the scope of standard EMS to improve the outcome of critically ill or severely injured patients. However, the impact of physician-staffed EMS on trauma patients is debated, and results from existing studies are contradictory(58, 132, 160, 161, 167, 168). A systematic review from 2009 revealed only a few controlled studies examining the effect of advanced interventions by a prehospital EMS physician on patient outcomes(167). An increased survival rate was found in major trauma patients and in patients with cardiac arrest. Differences among dispatch protocols, overall EMS organization, hospital treatment, methodology, and outcome measures make comparisons between studies difficult. Also, the variability in EMS team compositions and physician backgrounds complicates the comparison. For example, in the Anglo-American EMS system, only a minority of all HEMS units are staffed by EMS physicians(9).

It has been suggested that patients with TBI are also likely to benefit from EMS physicians treating or preventing possible insults leading to a secondary brain injury(58). Some studies suggest a beneficial impact on patient outcomes(161, 168-172), but not without contradictory results(132).

6.4.1 Patient characteristics

Large registry studies have revealed that TBI outcomes profoundly rely on demographic and trauma-related factors, such as age and secondary factors, mainly hypoxia and arterial hypotension(29, 55, 56).

Several studies have demonstrated that age has a prognostic value regarding TBI. Age has an effect on mortality independent from other factors(63). Two typical peaks for patients admitted with moderate to severe TBI exist in the 21-30 and 71-80 age groups(59). Patients older than 70 years have a higher mortality and worse functional outcomes(63, 64, 173, 174). The full extent of this impact is yet to be fully examined(64). The properties of an aging brain and its ability to heal, the typical types of brain injury related to the mechanism of the injury, or the effect of aging on the physiologic status could create a more severe injury(63, 65). It has also been suggested that the elderly mortality rate from head injuries is higher because less aggressive therapy is initiated in the earlier stages of treatment, but no clear evidence of this has been shown(59, 63). As noted earlier, the high incidence of comorbidities and the frequent use of platelet aggregation inhibitors and oral anticoagulants among older patients have a negative influence on TBI outcomes(21). The results of this thesis are comparable with these earlier findings.

In a review by Peeters(20), 13 out of 26 studies that provided data on the mechanisms of injury showed falls were the most frequent cause of TBI. RTAs were reported as the most frequent cause of TBI in 11 studies. Only two out of 12 studies from 2000 and later report RTAs as the main cause of brain injuries. In eight studies, falls were dominant. Thus, over time, a clear shift can be seen in the leading cause of TBI from RTAs to falls. Within the studies that focus on moderate-to-severe and severe TBI, RTAs remain the leading cause. A clear correlation was also found between age and the mechanism of the injury. Falls are most common in two age groups: the elderly and children. In contrast, RTAs are the most frequent cause of TBI in young adults. Also notable is the geographical spread of the mechanisms of the injury: Scandinavian countries mainly reported falls, while other countries reported more RTAs(20). This is consistent with all three TBI studies included in this thesis, as the main mechanisms of injury were falls and RTAs. The review by Peeters also reported males as the dominant gender in all 28 studies included(20), as was the case in our TBI studies.

It has been suggested that the dispatch of a physician-staffed EMS may increase the on-scene time, but at the time of this thesis, the effect of prehospital time frames on the outcomes of severe TBI patients(58, 129, 131-134) is unknown. It is likely different dispatch protocols, prehospital treatment strategies, and interventions (i.e., airway management) influence the on-scene time and, depending on the injury profile, impact the patients' outcomes. Prehospital time frames did not have an impact on the outcomes of TBI patients in studies II and III.

6.4.2 Comparison of outcomes in paramedic- versus physician-staffed EMS and introducing HEMS to a paramedic EMS system

The most profound difference in the prehospital treatment between paramedic-staffed and physician-staffed EMS in studies II and III was the definitive airway control by EMS physicians. In study II, hypoxia was common in the patients treated by the paramedic-staffed EMS on arrival to the ED, while in the patients treated by the physician-staffed EMS, almost none of the patients were hypoxic. The same result also occurred in study III. Hypoxemia is a strong predictor of the outcome in TBI, and the negative effect of hypoxemia on the outcome has been demonstrated in several studies(3, 4, 56, 92, 102). The likely explanation for this is the higher frequency of prehospital endotracheal intubation, controlled ventilation, and a more precise and invasive monitoring of the vital signs by EMS physicians. Anaesthetics were available for the EMS physicians, while the paramedics were limited to the use of sedatives, which might influence the rate of airway management procedures.

Early definitive airway control has become an established principle in the management and resuscitation of critically injured patients. It is considered to be the standard of care with TBI patients, as hypoxemia and hypercapnia can worsen brain injuries(103). As stated in the literature review, when considering the possible benefits of the prehospital endotracheal intubation of TBI patients, the literature is inconclusive. Some studies indicate benefits in survival, while others show increased mortality(37, 79, 105). Most studies are retrospective and study paramedics performing endotracheal intubation with a minimal use of sedative agents and muscle relaxants. Some studies indicate improved survival, while others show increased mortality(37, 79, 105). In the prehospital setting, endotracheal intubation has potential advantages: oxygenation can be optimized, and controlled ventilation is possible. The optimal prehospital way to secure the airway remains controversial(106, 175). If RSI is performed poorly, hypoxia and hypotension have been shown to have a negative effect on the outcomes of TBI patients(106). According to current knowledge, prehospital endotracheal intubation by EMS physicians is a safe procedure with low complication and high success rates(108-117).

6.4.3 Mortality and neurological outcomes

Prehospital GCS is reliable indicator of the severity of TBI(1). Mortality is increased and neurological outcomes are poorer in patients with low GCS scores. In particular, a GCS score of 3 at presentation has been associated with a significantly poor outcome(81-83). The results of study IV concur with these previous studies.

The prehospital TBI guidelines define hypotension as 90 mmHg in adults(1). The incidence of hypotension in patients with TBI upon first contact on-scene has been reported to be between 16–19 %(176, 177). As hypotension is common among TBI patients and has been associated with high mortality and poor functional outcomes(3, 77, 92-95), attention should be given to avoiding hypotension in the prehospital setting. A single episode of hypotension has been associated with a doubling of mortality and an increased morbidity when compared with a matched group of TBI patients without hypotension(3). In study IV's multivariable analyses, hypotension was a significant factor on mortality and a good neurological outcome.

The combined results of studies II-IV are strongly associated with a beneficial impact of the implementation of EMS physician interventions on TBI patient prognosis.

6.5 Strengths and limitations

This thesis has strengths and limitations that should be considered when interpreting the results. The individual studies were population-based retrospective studies with all the patients treated and cared for in the study university hospitals. Apart from study I, the included patients were recruited from the confirmed severe TBI diagnoses at discharge. The mortality data for all the studies were obtained from the national statistical authority Statistics Finland, which produces the Finnish official causes of death statistics.

The prehospital data were originally self-reported, could not be independently verified, and could have been biased as a result. Continuous data on vital signs covering the whole prehospital phase were not available; therefore, short-lived hypoxia or hypotension during the prehospital study periods cannot be excluded with certainty. Reliable pupil assessments were not recorded on all of the patients. It is possible the deaths occurring in the late stages of the follow-up period were unrelated to the prehospital index event, with secondary diseases or injuries being the cause. The outcome evaluations were based on patient record assessments without clinical examination or the help of a questionnaire. Neurosurgical and intensive care have advanced during the study period, which may also have affected the results.

6.6 Future perspectives

Mortality and morbidity reduction are essential after severe TBI, but improving neurological outcomes and the quality of life is important as well. The effectiveness of EMS systems and TBI treatments needs further attention, as the evidence is still lacking. Attention should also be given to continuous performance evaluations of EMS systems.

Prehospital studies are difficult to design. Multiple co-founders and interactions in the complex prehospital setting are hard to control and evaluate. Based on the results of this thesis, advanced prehospital treatment seems to be beneficial for severe TBI patients. Well-designed multicentre prospective studies with detailed data are needed to confirm the hypothesis that EMS physicians have a positive impact on the outcomes of TBI patients.

7 CONCLUSIONS

Based on these studies, the following conclusions can be drawn:

1. The overall prehospital one-year mortality of critically ill or severely injured patients treated on-scene by EMS physicians can be considered low.

2. Prehospital on-scene EMS physicians treating severe TBI patients are associated with lower mortality and better neurological outcomes.

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PUBLICATIONS

PUBLICATION
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One-year outcome after prehospital intubation

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One-year outcome after prehospital intubation

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Conflict of interest
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Background: The aim of physician staffed emergency medical services (EMS) is to supplement other EMS units in the care of prehospital patients. The need for advanced airway management in critical prehospital patients can be considered as one indicator of the severity of the patient's condition. Our primary aim was to study the long-term outcome of critically ill patients (excluding cardiac arrest) who were intubated by EMS physicians in the prehospital setting.
Methods: Data of 845 patients, whose airways were secured by the EMS physicians during a 5-year (2007–2011) period, were retrospectively evaluated. After exclusions, the outcome of 483 patients (8.9% of all patients treated by EMS) was studied. Evaluation was based on hospital patient records 1 year after the incident. For assessment of neurological outcome, a modified Glasgow Outcome Score (GOS) was used. Time and cause of death were recorded.
Results: 55.3% of the study patients had a good neurological recovery (GOS 4–5) with independent life 1 year after the event. The overall 1-year mortality (GOS 1) was 35.0%. Poor neurological outcome (GOS 2–3) was found in 9.7% of the patients. Patients with intoxication or convulsions survived best, while those with suspected intracranial pathology had the worst prognosis. Of all survivors, 85% recovered well.
Conclusion: The majority of the study patients had a favourable neurological recovery with independent life at 1 year after the incident. More than 80% of all deaths occurred within 30 days of the incident.

Editorial comment: what this article tells us
Prehospital endotracheal intubation is performed on varying indications and by different groups of personnel. Outcome depends probably on several factors in addition: e.g. indications, case mix and in-hospital treatment. In this study, the authors followed all critically ill patients intubated in the prehospital setting for 1 year after the incident. The large majority of mortality occurred within the first 30 days, although depending on diagnoses.

The aim of the physician staffed emergency medical service (EMS) is to provide advanced care and interventions beyond the scope of standard EMS to improve the outcome of critically ill or severely injured patients. The treatment of these patients in the prehospital setting often involves advanced airway management, which in such patients can be considered as one indicator

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of the severity of the patient's condition. According to current knowledge, prehospital endotracheal intubation by EMS physicians is a safe procedure with low complication and high success rates.[1–9]

The indications for prehospital endotracheal intubation performed by physician staffed EMS units have been reported in several studies.[1–8] The focus of earlier studies concerning patient outcome has mainly been on evaluating mortality rates and outcomes for trauma patients (in variable time frames) attended by physician staffed EMS.[1,9–13] Comprehensive data on long-term outcome are scarce. The overall care of the patient after advanced airway management, assuming that the procedure itself is uncomplicated, e.g. the support of ventilation and cardiovascular stability, probably influences the outcome more than endotracheal intubation itself.

Cardiac arrest patients differ from other critical prehospital patients in that advanced airway management does not require facilitating medication, and that the outcome of these patients depends on several other factors not related to the securing of the airway per se. In this subset of critical patients, the Utstein-style reporting template has been well established more than a decade ago.[14]

A recent European initiative suggested advanced airway management to be included in the top five research priorities for physician-provided prehospital care.[15] To our knowledge, no previous studies describe the long-term outcome of critical prehospital patients treated by an EMS physician.

Our primary aim was to study the long-term outcome of critically ill patients (excluding cardiac arrest) who were intubated by an EMS physician in the prehospital setting. Our secondary aim was to determine the indications and prehospital diagnosis leading to endotracheal intubation in these patients.

Material and methods

Description of the EMS system

The Helsinki area Helicopter Emergency Medical Service (HEMS) operates in the Uusimaa Hospital District surrounding the capital city of Helsinki in Southern Finland. It serves a population of 850,000 inhabitants, covers an area of 31,000 km^2 (100 km range) and responds to an average of about 2200 missions per year. The service is dispatched on primary missions together with ground EMS units to patients with potential major trauma or critical medical conditions. The Helsinki area HEMS unit is manned with a physician, a pilot and a flight medic 24 h a day. The physicians are dedicated anaesthesiologists with extensive experience in prehospital emergency medicine. The role of the helicopter is primarily to transport the physician to the scene, while patient transport is mainly carried out by EMS ground vehicles with the physician escorting the patient to the emergency department when necessary.

Study design

Prehospital airway management indications of critically ill or severely injured patients in the Helsinki area HEMS are based on international and national guidelines.[16,17] The data of all non-cardiac arrest patients whose airway was secured by the Helsinki area HEMS physician were analysed. As advanced airway management was used as an indicator of the severity of the patient's condition, we did not study the success rates of the technical procedures per se. Exclusion criteria are presented in Fig. 1.

During the study period (2007–2011), there was no standard operating procedure for prehospital intubation, and the pharmaceuticals facilitating the procedure were at the physician's discretion. The Helsinki area HEMS physician recorded prehospital treatment data on a run sheet, and the data were subsequently entered into an electronic database after each mission. Routinely collected data included physiological parameters, intubation related variables including the possible need for a surgical airway, other interventions and drugs used during the mission.

The study patients were identified from the Helsinki area HEMS electronic database. Age, gender, airway-related variables, along with data on hospital treatment and primary outcome evaluation were reviewed and cross-referenced with the run sheets. The patients' post-incident status was determined from hospital records. The outcome evaluation was performed by one of the authors (T. Pakkanen) based on hospital patient records 1 year after the incident. In case of

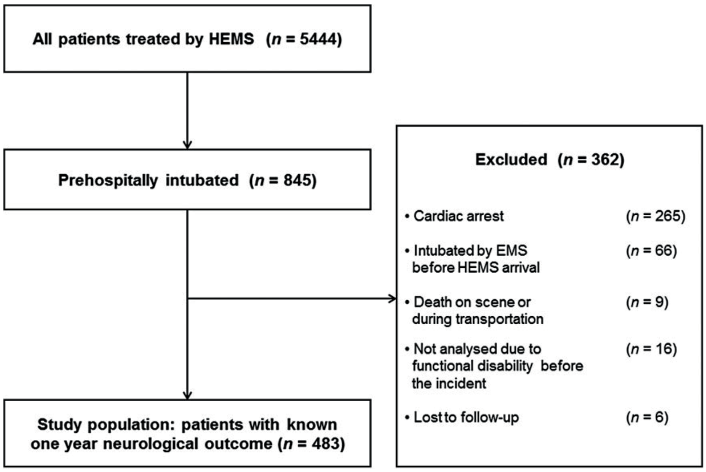


Fig. 1. Flowchart.

missing patient medical records or if the evaluation was unclear, the research team members either reviewed the case and a joint decision was made, or outcome was marked as 'lost to follow-up' (Fig. 1).

For assessment of neurological outcome, a modified Glasgow Outcome Score (GOS) was used.[18] A GOS of 1 denoted death within a year, GOS 2–3 poor neurological outcome (need for assistance in activities of daily life) and GOS 4–5 suggested a good neurological recovery (independent life). Data on the time and cause of death were obtained from Statistics Finland.[19] Patients with a known need for personal assistance in activities of daily life prior to the incident leading to prehospital intubation were excluded from the outcome evaluation, since outcome evaluation was not considered feasible in these cases (Fig. 1).

The study protocol was approved by, and permission to conduct the study was obtained from the Coordinating Research Director of the Helsinki University Hospital (date: 23 August 2010, ClinicalTrials.gov ID NCT02307123). The study was observational in nature, and classified as a service evaluation retrospectively analysing routinely collected data; therefore, the Ethics Committee approval was not considered mandatory at the Helsinki University Hospital.

The data were analysed using IBM SPSS Statistics for Windows (Version 21.0; IBM Corp., Armonk, NY, USA). Results are expressed as medians and ranges or percentages. A Kaplan–Meier survival curve illustrates the survival in different prehospital diagnosis.

Results

During the 5-year study period, the Helsinki area HEMS attended 5444 patients. Of these, 845 patients (15.5%) had their airway secured in the prehospital setting. After exclusions, the data of 483 patients (8.9%) met the inclusion criteria for the present study, and were further analysed (Fig. 1). The data of nine primary non-cardiac arrest patients (seven trauma, two non-trauma), who died after prehospital intubation but before hospital admission and who were therefore excluded, are given in Table 1.

The median age of the study patients was 47.8 years (range 0.1–90.7 years); 66% were male. Females were more represented in the elderly age groups (defined as above 70 years of age). Good neurological recovery (GOS 4–5; i.e., ability to live an independent life) was found in 55.3% of the patients. The overall 1-year mortality (GOS 1) was 35.0%, while poor neurological outcome (GOS 2–3) was documented in 9.7% of the patients. Of all survivors, 85.0% recovered well. The majority of the patients in the younger age groups (below 60 years of age) recovered neurologically well. The probability to die increased by age, odds ratio = 1.05 (95% confidence interval 1.04–1.06) (Fig. 2).

The main indication for endotracheal prehospital intubation in the study population was decreased level of consciousness without trauma (53.2%) or due to trauma (37.9%). Other indications were a minority, as they covered altogether less than 10% of the cases (Fig. 3).

The primary Glasgow Coma Scale (GCS) on-scene was ≤8 in 82.8%, 9–13 in 11.5% and 14–15 in 5.7% of the patients. In the patients with initial GCS 9–15, the airway was secured due to respiratory failure ($n = 11$), intracranial pathology with decreasing consciousness ($n = 9$), head trauma ($n = 8$), major burn ($n = 8$), facial or neck trauma ($n = 7$), need of analgesia ($n = 7$) or intoxication ($n = 4$).

The Helsinki area HEMS physician's main prehospital diagnoses were trauma with isolated or concomitant head injury (32.9%), suspected spontaneous intracranial pathology (21.7%), intoxication (13.3%) and convulsions (9.3%). Males were most often suspected to have decreased level of consciousness due to isolated or concomitant head injury (36.2%), whereas in females, the most frequent prehospital diagnosis was spontaneous intracranial pathology (28.5%).

Of the study patients who died, 42.6% died within the first 24 h, with an additional 25.3% in a week, and 81.7% deaths occurred within the first 30 days after the incident. Patient survival in relation to prehospital diagnosis is presented in Fig. 4. The most favourable outcome was found in patients with intoxication or convulsions as the prehospital diagnosis, while those with intracranial pathology had the worst survival rate (Table 2).

Discussion

Our observational study showed that more than half of the patients, whose airways were secured

Table 1 Deaths on-scene or before hospital admission ($n = 9$).

Prehospital diagnosis	Primary on-scene GCS
Head trauma (motor vehicle collision)	3
Head and thorax trauma (motor vehicle collision)	3
Thorax and abdomen trauma (motor vehicle collision)	13
Head and thorax trauma (fall from heights)	3
Head and thorax trauma (fall from heights)	3
Hypovolemia (stabbing)	Missing data
Hypovolemia (major wound; patient not accessible)	15
Hypovolemia (haematemesis)	14
Respiratory failure	12

GCS, Glasgow Coma Scale.

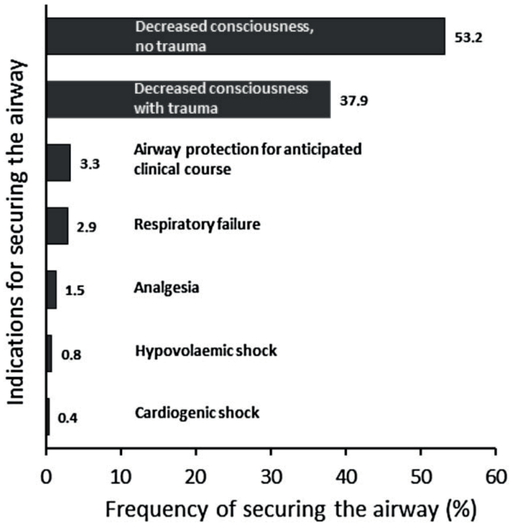


Fig. 3. Indications for prehospital intubation in per cents.

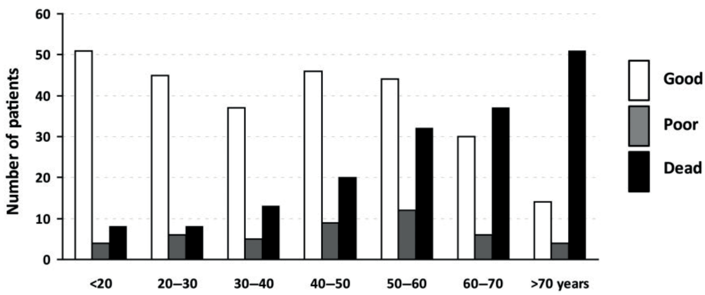
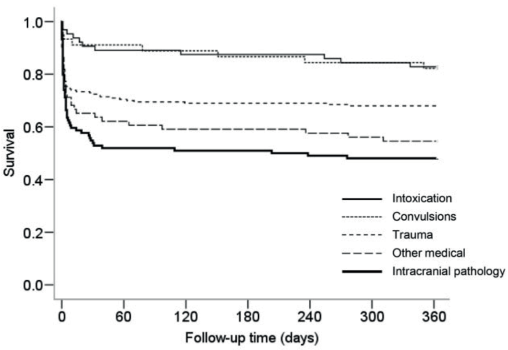


Fig. 2. One-year outcome in relation to age.



	n	Survival rate Day 180	Survival rate Day 365
Intoxication	64	0.875	0.828
Convulsions	45	0.867	0.822
Trauma	203	0.690	0.680
Other medical	66	0.591	0.545
Intracranial pathology	105	0.505	0.476

Fig. 4. One-year survival in relation to prehospital diagnoses. Other medical: undefined coma ($n = 32$); respiratory failure ($n = 17$); cardiogenic shock ($n = 6$); septicemia ($n = 5$); hypoglycemia ($n = 3$); airway obstruction ($n = 2$); hypovolemic shock ($n = 1$).

Table 2 Outcome in different prehospital diagnoses in percentages ($n = 483$).

Prehospital diagnosis		One-year neurological outcome Good	Poor	Death
Intoxication	($n = 64$)	82.8%	0%	17.2%
Convulsions	($n = 45$)	77.8%	4.4%	17.8%
Trauma	($n = 203$)	53.2%	14.8%	32.0%
Other medical	($n = 66$)	48.5%	6.0%	45.5%
Intracranial pathology	($n = 105$)	37.2%	10.5%	52.3%

Other medical: see Fig. 4.

in the prehospital setting and who were thereafter admitted to hospital, had a favourable long-term neurological recovery: they lived an independent life 1 year after the incident. The total 1-year mortality was 35%, which most likely reflects the critical conditions leading to prehospital intubation. As the Kaplan–Meier curve in Fig. 4 indicates, in these patients, the primary diagnosis was probably the major determinant influencing long-term survival. However, the study population appeared to divide into several subgroups: while the 1-year survival of the patients with intoxications or convulsions was more than 80%, respectively, of those with intracranial pathology more than half died. Interestingly, in all subgroups, the initial mortality rate was high, and over 80% of all deaths occurred during the first 30 days after the incident. Thus, our results suggest that the previous studies reporting 30-day mortality will give a reasonable, although not absolutely accurate estimate of the long-term survival.

The creators of GOS concluded in their later studies that it was exceptional for a traumatic brain injury (TBI) patient who was severely disabled at 3 months after the injury ever to reach the category of good recovery.[20] Their studies also showed that the majority of patients had reached their final outcome category within 6 months of injury, and that very few changed category after a year. Our definition for the ‘long-term’ follow-up period of 1 year was based on the finding that very few patients change GOS rating after a year.

Comparison of our results with those from other studies is difficult. In many previous studies, the investigators have evaluated trauma patients[9,12,13] with a special focus on TBI.[10–12] In these studies, the mortality rates have been reported either as the discharge[9,12] or 30-day mortality.[13] Subgroups like those with the worst prognosis in our analysis, i.e. ‘other medical’ or ‘intracranial pathology’ are typically missing in studies. Therefore, a reliable comparison is difficult to make. It is noteworthy, however, that in our study, the mortality was only moderate between 30 and 365 days after the incident, probably reflecting the natural course of the illness. Other earlier prehospital intubation studies on patient outcome have mainly reported TBI patient survival and neurological outcome in paramedic-based EMS systems.[21–23]

Rognås et al.[1] conducted a prospective descriptive study including patients from all age groups and all prehospital endotracheal intubation indications in Denmark and reported a 30-day mortality of 48.9%. The mortality rate in that study carried a degree of uncertainty, because, according to the authors of the study, part of the in-hospital mortality data were missing in about one third of the cases due to a change of hospital patient record systems. Their study also included cardiac arrest patients and those who died in the prehospital setting.

The Helsinki area HEMS physician’s three main prehospital diagnoses in our patients were trauma with isolated or concomitant head injury, suspected intracranial pathology and intoxication, which all have a high probability to lead to a decreased level of consciousness. While the prehospital diagnoses in other studies have been quite similar, variation also occurs between different physician-staffed EMS systems.[5,7,8,10–12] Some units focus on preselected patients groups (e.g. trauma patients), and different dispatch criteria may also explain the difference.

The majority of our patients had a low primary GCS (3–8) as expected, which agrees with earlier studies.[1,3,8–10] The main indication for prehospital endotracheal intubation in the Helsinki area HEMS in non-cardiac arrest patients was decreased level of consciousness with or without trauma, followed by airway protection for anticipated clinical course, and respiratory distress. This concurs with previous studies reporting main indications for prehospital intubation to be decreased level of consciousness, respiratory distress or exhaustion and compromised airway.[1–8]

Study limitations

The prehospital data were originally self-reported and can therefore be biased. Although the missions were routinely recorded in the database on a daily basis and the study data were cross-referenced with the original run sheets, the database was not originally designed for this study and the reported data could not be independently verified. The outcome evaluation was made by the authors based on patient record assessment without physical examination or the help of a questionnaire. The outcome of a small group of patients who were lost for follow-up could not be evaluated. Finally, we were unable to match the post-mortem diagnoses with the initial prehospital diagnoses. Therefore, it is possible that the deaths occurring at the late phases of the follow-up period were unrelated to the prehospital index situations and secondary diseases or injuries could have influenced patient survival and outcome during the follow-up period.

Conclusions

Based on this study, the long-term outcome of critical patients treated with endotracheal intubation in the prehospital setting may be considered relatively good. The majority of the patients had a favourable neurological recovery with independent life at 1-year after the incident leading to prehospital endotracheal intubation irrespective of the indication for the intervention. Even though the mortality rate was notably high, 85% of the survivors recovered well.

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PUBLICATION
II

Pre-hospital severe traumatic brain injury - comparison of outcome in paramedic versus physician staffed emergency medical services

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ORIGINAL RESEARCH — Open Access

Pre-hospital severe traumatic brain injury – comparison of outcome in paramedic versus physician staffed emergency medical services

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Abstract

Background: Traumatic brain injury (TBI) is one of the leading causes of death and permanent disability. Emergency Medical Services (EMS) personnel are often the first healthcare providers attending patients with TBI. The level of available care varies, which may have an impact on the patient's outcome. The aim of this study was to evaluate mortality and neurological outcome of TBI patients in two regions with differently structured EMS systems.

Methods: A 6-year period (2005 – 2010) observational data on pre-hospital TBI management in paramedic-staffed EMS and physician-staffed EMS systems were retrospectively analysed. Inclusion criteria for the study were severe isolated TBI presenting with unconsciousness defined as Glasgow coma scale (GCS) score ≤ 8 occurring either on-scene, during transportation or verified by an on-call neurosurgeon at admission to the hospital. For assessment of one-year neurological outcome, a modified Glasgow Outcome Score (GOS) was used.

Results: During the 6-year study period a total of 458 patients met the inclusion criteria. One-year mortality was higher in the paramedic-staffed EMS group: 57 % vs. 42 %. Also good neurological outcome was less common in patients treated in the paramedic-staffed EMS group.

Discussion: We found no significant difference between the study groups when considering the secondary brain injury associated vital signs on-scene. Also on arrival to ED, the proportion of hypotensive patients was similar in both groups. However, hypoxia was common in the patients treated by the paramedic-staffed EMS on arrival to the ED, while in the physician-staffed EMS almost none of the patients were hypoxic. Pre-hospital intubation by EMS physicians probably explains this finding.

Conclusion: The results suggest to an outcome benefit from physician-staffed EMS treating TBI patients.

Trial registration: ClinicalTrials.gov ID NCT01454648

Keywords: Pre-hospital Emergency Care (MeSH), Emergency Medical Services (MeSH), Critical Care (MeSH), Traumatic Brain Injury (MeSH), Airway Management (MeSH), Endotracheal Intubation (MeSH), Patient Outcome Assessment (MeSH), Glasgow Outcome Scale (MeSH)

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Background

Worldwide, traumatic brain injury (TBI) is one of the leading causes of death and permanent disability [1] particularly in young adults. After the initial injury, many patients suffer secondary brain injuries because of hypoxia, hypercapnea and hypotension. The secondary brain injuries can result in increased mortality and disability [1].

The management of severe TBI focuses on the prevention of secondary ischemic brain injury by optimizing the balance between cerebral oxygen delivery and utilization [2, 3]. Cerebral oxygen delivery is partly determined by the arterial oxygen content and partly by cerebral blood flow (CBF), and therefore is affected by cerebral autoregulation. When the autoregulation is impaired, a correlation between mean arterial pressure (MAP) and CBF exists, making the brain susceptible to ischemia or hyperemia [4, 5].

Half of those who die from TBI do so within the first two hours of injury [1]. Emergency Medical Services (EMS) personnel are often the first healthcare providers attending patients with TBI [1]. Thus, pre-hospital assessment and treatment is a critical link in providing appropriate care [6] as the prognosis of patients with severe TBI and low Glasgow Coma Scale (GCS) score depends strongly on early support of vital functions [3, 7]. In particular, pre-hospital prevention of hypoxia by adequate respiratory management including secured airway, normoventilation and prevention of aspiration is strongly associated with improved outcome [8–11]. Depending on the structure of the EMS system, the level of available care varies, which may have an impact on the patient's outcome.

The aim of this study was to evaluate mortality and neurological outcome of TBI patients in two regions with differently structured EMS systems.

Methods

Description of the EMS system

Finland covers an area of 337,000 km2 with a population of 5.4 million. Half of the population lives in the south, whereas the middle and especially northern parts of the country are rural. In larger cities, the fire brigade is the usual EMS provider, whereas private entrepreneurs are most frequent in rural areas. The EMS system in general is three-tiered: basic life support (BLS), advanced life support (ALS) and physician-staffed units. Rescue department fire engines can also be used as first responders. BLS units are usually manned with fire fighters and authorized to use for example an automated external defibrillator (AED), perform tracheal intubation of a lifeless adult patient and to establish an intravenous line. The advanced level employs nurses and paramedics with 3.5 – 4 years of training who are authorized e.g. to give intravenous drugs, provide sedation to facilitate tracheal intubation in unconscious patients and initiate thrombolytic treatment after consulting with a physician. In cities, response times for basic units average 5–7 min, ALS response times vary between 10 and 15 min. Physician-staffed ground vehicles are used in two cities and five helicopter based physician-staffed units cover other parts of the country. The physician-staffed unit calls are not restricted to trauma as they respond to medical emergencies as well.

The Pirkanmaa area paramedic-staffed EMS system (EMS)

The Pirkanmaa Hospital District is situated in Western Finland. There are approximately 200 000 inhabitants living in the city of Tampere and another 250 000 inhabitants in the surrounding communities. At the time of the study, there were no dedicated medical directors, and EMS crews consulted on-call hospital physicians and local general practitioners for treatment guidelines. Physician-staffed pre-hospital units and on-line medical supervision were not available. Paramedic-staffed EMS units provided pre-hospital care in this region. During the study period, patients with a decreased level of consciousness were routinely administered oxygen according to national guidelines. Neuromuscular blocking agents were not available in the pre-hospital service and pre-hospital advanced airway management was performed using sedatives and opioids only.

The Helsinki and Uusimaa area physician-staffed EMS system (Ph-EMS)

The Helsinki and Uusimaa Hospital District is situated in the southern part of Finland with a total of 1.3 million inhabitants living in the capital area. During the study period, the hospital district's EMS system was a three-tiered system with two physician-staffed units: a physician-staffed mobile intensive care unit (MICU) and a Helicopter Emergency Medical Service (HEMS) unit providing the third tier. Patients with a decreased level of consciousness were routinely administered oxygen according to national guidelines. The physician-staffed EMS units were dispatched on primary missions together with basic or advanced life support EMS units to patients with potential major trauma or critical medical conditions. The physicians are dedicated anaesthesiologists with extensive experience in pre-hospital emergency medicine. In the physician-staffed units, general anaesthesia including neuromuscular blocking agents could be used to facilitate rapid sequence intubation (RSI).

Neurosurgical care

Within both study areas, a university hospital operated as the referral centre providing standardized immediate neurosurgical care according to national guidelines (the first edition published in 2003, with an update in 2008). Both facilities operate according to similar treatment principles, in terms of criteria for surgical interventions and timing of surgery.

Study design

A 6-year period (2005–2010) observational data on pre-hospital severe TBI management in both EMS systems were retrospectively analysed. Patients included in the study were identified from the university hospital patient records based on the ICD-10 discharge diagnoses for traumatic brain injury or for skull fracture (S06.2-S06.6, S06.8, S02.1). Inclusion criteria for the study were severe isolated TBI presenting with unconsciousness defined as Glasgow coma scale (GCS) score ≤8 [12] occurring either on-scene, during transportation or verified by an on-call neurosurgeon at admission to the hospital. Patients with concomitant multiple injuries with the need for surgical interventions (other than neurosurgery) were excluded, as were patients transferred from other hospitals (secondary transfers). Desaturation was defined as a decrease in SpO_2 to below 90 %. Hypotension was defined as a decrease in systolic blood pressure (SBP) below 90 mmHg. These definitions are consistent with the latest edition of the Brain Trauma Foundation's guidelines for pre-hospital management of traumatic brain injury [1].

Age, gender, EMS response and total mission time, airway related variables, mechanism of injury, GCS score and vital signs at the scene and on arrival to the emergency department (ED) were reviewed and cross-referenced with EMS run-sheets and ED documentation. Outcome evaluation was performed based on hospital patient records one year after the incident. In multivariable analysis, hypoxia and hypotension were used as risk factors for mortality based on previous studies [3, 7] as well as age and GCS score based on them being among the core variables in the IMPACT [13] and CRASH [14] prognostic TBI models.

For assessment of neurological outcome, a modified Glasgow Outcome Score (GOS) was used [15]. A GOS of 1 denoted death within a year, GOS 2–3 poor neurological outcome (need for assistance in activities of daily life) and GOS 4–5 corresponded to good neurological recovery (independent life). The outcome evaluation was performed by one of the authors (T.P.) based on hospital patient records six months after the incident. If the evaluation was unclear, the research team members reviewed the case and a joint decision was made. Data on the time of death were obtained from the national statistical authority Statistics Finland.

The study was approved by Regional Ethics Committee of the Pirkanmaa Hospital District (R09161), permission to conduct the study was obtained from the Research Directors of Tampere and Helsinki University Hospitals and the study was registered in ClinicalTrials.gov (Identifier NCT01454648).

Statistical analyses

Results are expressed as medians and ranges or percentages. EMS groups were compared using chi-square or Fishers exact test for categorical variables. The odds ratios and 95 % confidence intervals were calculated using univariate and multivariable binary logistic regression to identify predictors of good neurological outcome and one-year mortality. The one-year survival was characterized using Kaplan-Meier plot and the log-rank test was used to compare groups. Statistical significance was considered at a value of less than 0.05. The data were analysed using IBM SPSS Statistics for Windows Version 21.0. Armonk, NY: IBM Corp. Released 2012.

Results

During the 6-year study period a total of 458 patients met the inclusion criteria (Fig. 1). The complete data of 181 patients in the EMS and 270 patients in the Ph-EMS were available for final neurological outcome analysis. The baseline characteristics are presented in Table 1.

The time from dispatch to the arrival of the first EMS unit on-scene did not differ between the groups: the median response time was 8 (range 0–37) minutes in the EMS and 9 (range 0–62) minutes in the Ph-EMS groups ($p = 0.246$). However, the total mission times (from dispatch to arrival to ED) were shorter in the EMS group: median time of 54 (range 18–180) minutes compared to Ph-EMS group 72 (range 23–191) minutes ($p < 0.001$).

First recorded systolic blood pressure on-scene was hypotensive (<90 mmHg) in 4 % in the EMS treated group, and hypoxia (SpO_2 <90 %) was documented in 19 % of the patients. The corresponding figures in the Ph-EMS treated patients were 3 % ($p = 0.44$) and 15 %, ($p = 0.31$), respectively. Advanced airway management was performed in 16 % of the patients in the EMS group and in 98 % of the patients in the Ph-EMS group ($p < 0.001$). Details on airway management are described in Table 2. On arrival to ED, hypotension was recorded in 4 % in both study groups but the patients in the EMS group were more often hypoxic (10 % vs. 1 %, OR 10.05 CI 2.91–34.67, $p < 0.001$). Outcome by secondary insult at the time of arrival at ED is presented in Table 3.

One-year mortality was higher in the EMS group: 57 % vs. 42 % (OR 1.86 CI 1.27–2.71, $p = 0.001$). Good neurological outcome was less common in patients treated in the EMS group: 32 % of the EMS and 38 % (OR 0.74 CI 0.5–1.11, $p = 0.14$) of the Ph-EMS treated

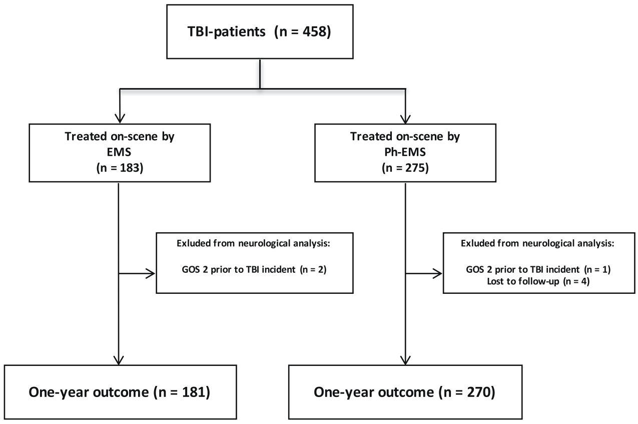

Fig. 1 Flowchart

patients had a good neurological recovery (GOS 4–5) with independent life one year after the event. In the multivariable analysis after the patients were adjusted by age (OR 1.05 CI 1.04–1.07, p <0.001), the EMS-system remained as a significant risk factor for mortality (OR 1.69 CI 1.11–2.58, p = 0.015). Long-term mortality of the two patient groups is illustrated in Fig. 2.

Discussion

In this observational retrospective study the results point to outcome benefit from physician-staffed EMS treating TBI patients. Mortality was significantly lower and neurological outcome better in patients in the physician-staffed EMS group compared to the paramedic-staffed EMS group.

Pre-hospital advanced airway management of TBI patients is well defined in international guidelines: an airway should be established in patients who have severe TBI (GCS ≤8), have the inability to maintain an adequate airway or are hypoxemic, which is not corrected by supplemental oxygen by the most appropriate means available [1]. In the pre-hospital setting endotracheal

Table 1 Baseline characteristics

	EMS		Ph-EMS		
	n = 183		n = 275		
	mean	SD, range	mean	SD, range	p-value
Age, years	52	21.6, 6–89	47	19.7, 0.2–90	0.014
	n	%	n	%	
Male	127	69	204	74	0.263
Mechanism of injury					0.018
Fall from ground level	81	44	105	38	
Traffic accident	41	22	51	19	
Fall from a height (>2 m)	25	14	36	13	
Violence	14	8	24	9	
Other	4	2	25	9	
Unknown	18	8	34	12	
Primary GCS					
Median	4	-	4	-	0.370
≤8	137	75	247	90	
9–13	13	7	14	5	
14–15	6	3	7	3	
Unknown	27	15	7	3	

Table 2 Pre-hospital airway management

	EMS		Ph-EMS		
	n	%	*n*	%	*p*-value
Airway secured	29	16	269	98	<0.001
Intubation (drug-facilitated)	19	10	263	96	
Intubation (without medication)	6	3	0	0	
Supraglottic device	4	2	5	2	
Surgical airway	0	0	1	0	
Not secured	154	84	6	2	
Failed pre-hospital intubation attempt(s)	3	2	0	0	

intubation has potential advantages: oxygenation can be optimised and controlled ventilation is possible with the airway secured. The optimal way of securing the airway still remains controversial [16, 17]. If RSI is performed poorly, hypoxia and hypotension have been shown to have a negative effect on outcome of TBI patients undergoing pre-hospital RSI [17].

In this study, the airway was secured in the pre-hospital setting in almost all of the patients in the physician-staffed EMS group and only in few patients in the paramedic-staffed EMS group. Anaesthetics were available for the EMS physicians, while the paramedics were limited to the use of sedatives only, which might have an effect on the rate of airway management procedures.

In earlier studies both hypoxemia and hypotension have been shown to have a negative impact on outcome [3, 8]. Desaturations (SpO_2 <70 %) during intubation or any oxygen desaturation (SpO_2 <90 %) has been associated with higher mortality [17]. The incidence of hypotension in patients with TBI upon first contact in the field has been reported to be between 16–19 % [18, 19]. A single episode of hypotension has been associated with increased mortality when compared with a matched group of patients without hypotension [3].

We found no significant difference between the study groups when considering the secondary brain injury associated vital signs on-scene. Also on arrival to ED, the proportion of hypotensive patients was similar in both groups. However, hypoxia was common in the patients treated by the paramedic-staffed EMS on arrival to the ED, while in the physician-staffed EMS almost none of the patients were hypoxic. Pre-hospital intubation by EMS physicians probably explains this finding. Detailed data on vital signs covering the whole pre-hospital phase in the study groups were not available in this retrospective study, so the presence of momentary hypoxia or hypotension during the pre-hospital period could not be further evaluated.

Due to the low rate of intubation in the paramedic-staffed EMS group, ventilatory parameters could not be compared. Arterial blood gas results from the ED were documented in 85 % of the physician EMS group and in 48 % of the paramedic EMS group. When analysing this further we found that only 36 % of the arterial blood gas samples in the physician EMS group and 14 % in the paramedic EMS group were analysed within 10 min or less after arrival to the ED and would in our opinion represent the oxygenation and ventilation during the pre-hospital phase. Therefore no further analysis was made.

There were no differences between the groups in gender, mechanism of injury, EMS response times or initial GCS. When the patient groups were adjusted by age, the EMS-system still remained as a significant variable in multivariable regression analysis of mortality risk factors.

The finding that the physician EMS group produced more patients with poor neurological outcome, can possibly be explained by Stoccheti's hypothesis: "The quality of the overall trauma system affects the outcome of the series because a better trauma system produces less favourable outcomes. This apparent paradox is due to the fact that a more efficient trauma system brings even the most severe cases to the hospital" [20].

Study limitations

This was an observational retrospective study and some limitations should be considered when interpreting the results. The pre-hospital data were originally self-reported and could not be independently verified and

Table 3 Outcome by secondary insult at the time of arrival at ED

	EMS					Ph-EMS				
Secondary			Outcome					Outcome		
Insult	*n*	%	Good	Poor	Dead	*n*	%	Good	Poor	Dead
Neither	149	86.6	33.6 %	10.7 %	55.7 %	246	94.6	38.6 %	17.5 %	43.9 %
Hypoxia	17	9.9	23.5 %	17.6 %	58.8 %	4	1.5	25.0 %	0 %	75.0 %
Hypotension	5	2.9	40.0 %	20.0 %	40.0 %	10	3.9	10.0 %	40.0 %	50.0 %
Both	1	0.6	0 %	0 %	100 %	0	0	0 %	0 %	0 %
Total	172	100	32.6 %	11.6 %	55.8 %	260	100	37.3 %	18.1 %	44.6 %
Data not available for 9 patients.						Data not available for 10 patients.				

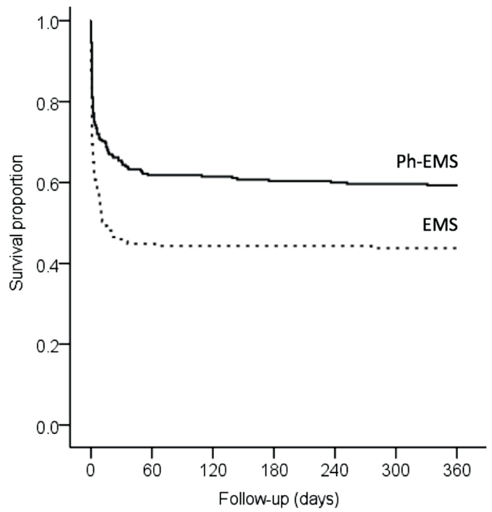

Fig. 2 One-year survival in relation to EMS system

can therefore be biased. When considering the age distribution, the groups were not originally identical. Reliable pupil assessment was not recorded on all of the patients. Complete data on vital signs covering the prehospital phase were not available for all patients. The outcome evaluation was based on patient record assessment without physical examination or the help of a questionnaire. The first CT scans were not evaluated using the Marshall classification. It is possible that the deaths occurring at the late phases of the follow-up period were unrelated to the pre-hospital index situations and secondary diseases or injuries could have influenced patient survival and outcome during the follow-up period.

Conclusions

Based on available data, the results suggest to an outcome benefit from physician-staffed EMS treating TBI patients. Further prospective multicentre studies with more thoroughly data of vital signs covering the prehospital phase, total pre-hospital treatment and the outcome evaluation are needed to confirm the hypothesis.

Abbreviations

ED: emergency department; EMS: emergency medical services; GCS: Glasgow coma scale; GOS: Glasgow outcome score; HEMS: helicopter emergency medical service; MICU: mobile intensive care unit; RSI: rapid sequence intubation; TBI: traumatic brain injury.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

TP: the concept and design of the study, acquisition and evaluation of the data and main writer. IV: the concept and design of the study, evaluation of the data and the manuscript. AK: evaluation of the data and the manuscript. HH: statistical analyses and evaluation of the data. TS: the concept and design of the study, evaluation of the data and the manuscript. JV: evaluation of the data and the manuscript. TR: evaluation of the data and the manuscript. AYH: evaluation of the data and the manuscript. All authors read and approved the final manuscript.

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This study is dedicated to the memory of Janne Virta, M.D.

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PUBLICATION
III

Physician-staffed helicopter emergency medical service has a beneficial impact on the incidence of prehospital hypoxia and secured airways on patients with severe traumatic brain injury

Pakkanen T, Kämäräinen A, Huhtala H, Silfvast T, Nurmi J, Virkkunen I, Yli-Hankala A

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ORIGINAL RESEARCH

Open Access

Physician-staffed helicopter emergency medical service has a beneficial impact on the incidence of prehospital hypoxia and secured airways on patients with severe traumatic brain injury

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Abstract

Background: After traumatic brain injury (TBI), hypotension, hypoxia and hypercapnia have been shown to result in secondary brain injury that can lead to increased mortality and disability. Effective prehospital assessment and treatment by emergency medical service (EMS) is considered essential for favourable outcome. The aim of this study was to evaluate the effect of a physician-staffed helicopter emergency medical service (HEMS) in the treatment of TBI patients.

Methods: This was a retrospective cohort study. Prehospital data from two periods were collected: before (EMS group) and after (HEMS group) the implementation of a physician-staffed HEMS. Unconscious prehospital patients due to severe TBI were included in the study. Unconsciousness was defined as a Glasgow coma scale (GCS) score ≤ 8 and was documented either on-scene, during transportation or by an on-call neurosurgeon on hospital admission. Modified Glasgow Outcome Score (GOS) was used for assessment of six-month neurological outcome and good neurological outcome was defined as GOS 4–5.

Results: Data from 181 patients in the EMS group and 85 patients in the HEMS group were available for neurological outcome analyses. The baseline characteristics and the first recorded vital signs of the two cohorts were similar. Good neurological outcome was more frequent in the HEMS group; 42% of the HEMS managed patients and 28% ($p = 0.022$) of the EMS managed patients had a good neurological recovery. The airway was more frequently secured in the HEMS group ($p < 0.001$). On arrival at the emergency department, the patients in the HEMS group were less often hypoxic ($p = 0.024$). In univariate analysis HEMS period, lower age and secured airway were associated with good neurological outcome.

Conclusion: The introduction of a physician-staffed HEMS unit resulted in decreased incidence of prehospital hypoxia and increased the number of secured airways. This may have contributed to the observed improved neurological outcome during the HEMS period.

Trial registration: ClinicalTrials.gov IDNCT02659046. Registered January 15th, 2016.

Keywords: Prehospital emergency care (MeSH), Emergency medical services (MeSH), Critical care (MeSH), Traumatic brain injury (MeSH), Airway management (MeSH), Endotracheal intubation (MeSH), Patient outcome assessment (MeSH), Glasgow outcome scale (MeSH)

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Introduction

After traumatic brain injury (TBI), hypotension, hypoxia and hypercapnia have been shown to result in secondary brain injury that can lead to increased mortality and disability [1]. As the prognosis of patients with severe TBI and a low Glasgow Coma Scale (GCS) score depends on early support of vital functions [2, 3], effective prehospital assessment and treatment is considered essential for favourable outcome [4]. In particular, prehospital prevention of hypoxia by adequate airway and respiratory management including a secured airway, normoventilation and prevention of aspiration is strongly associated with improved outcome [5–8].

Depending on the structure of the emergency medical service (EMS) system the level of available treatment varies, and this may have an impact on the patient's outcome. A systematic review from 2009 revealed only a few controlled studies examining the effect of advanced interventions by a prehospital EMS physician on outcome. Increased survival was found in major trauma patients and in patients with cardiac arrest [9].

Although a Helicopter Emergency Medical Service (HEMS) is a part of the prehospital trauma system in many countries, HEMS and the possible impact it has on outcome in traumatically injured patients remains a subject of debate. Studies have been performed with the aim to evaluate the effect of HEMS on outcome in trauma patients, with contradictory results [10–15]. Differences in HEMS team composition, dispatch protocols, EMS organisation, hospital treatment and methodology and outcome measures make comparisons between studies difficult.

The aim of this study was to evaluate the effect of a physician-staffed HEMS in the treatment of TBI patients. The hypothesis was that implementation of a physician-staffed HEMS would have a positive effect on outcome.

Material and methods

The Pirkanmaa district has the second largest population in Finland, with approximately a half million inhabitants living in the city of Tampere and in the surrounding municipalities. All TBI patients in the study region are admitted to Tampere University Hospital, which is the referral centre in the area, and provides immediate neurosurgical care according to national guidelines (the first edition published in 2003, with an update in 2008) [16].

Period 1 (2005–2010): Paramedic EMS (EMS group)

The EMS was the responsibility of and organised by each of the municipalities in the region. The system was two-tiered, with emergency medical technician basic life support and paramedic advanced life support units. There were no dedicated on-call EMS medical directors, and no physician-staffed EMS units available on-scene. Prehospital crews consulted on-call hospital and local primary care physicians for treatment guidelines when deemed necessary. Patients with a decreased level of consciousness were routinely administered oxygen according to national guidelines and ventilation was assisted with bag-valve mask if required. Endotracheal intubation was primarily performed in cardiac arrest patients and infrequently in patients with a decreased level of consciousness. Hypnotics or neuromuscular blocking agents were not available in the prehospital setting and endotracheal intubation was performed using sedatives and opioids only, at the discretion of the paramedic on the scene.

Period 2 (2012–2015): Physician-staffed HEMS (HEMS group)

A physician-staffed HEMS was introduced into the EMS in the autumn of 2011, covering all municipalities in the study area. The HEMS is dispatched on primary missions together with basic or advanced life support EMS units to patients with potential major trauma or other critical medical condition. The role of the helicopter is primarily to transport the physician to the scene, while patient transport is mainly carried out by EMS ground vehicles with the physician escorting the patient to the emergency department (ED) when necessary. The physicians are anaesthesiologists experienced in prehospital critical emergency medicine and conduct advanced airway management according to the HEMS unit TBI standard operation procedure (SOP). General anaesthesia complying with the principles of neuroanaesthesia, including hypnotics, opioids and neuromuscular blocking agents, is routinely used for rapid sequence intubation (RSI). Capnography-assisted controlled ventilation, invasive haemodynamic monitoring with arterial blood gas sampling and, if necessary, noradrenaline-infusion and hypertonic saline are also routinely employed according to the unit's TBI SOP and national guidelines [16].

Study design

This retrospective cohort study compares the outcome of patients with severe TBI. Prehospital data from two periods were collected: before (EMS group) and after (HEMS group) the implementation of the HEMS. Data of the EMS group have been presented in a previous study [10] comparing the outcome of TBI patients in two differently structured EMS systems and were used as a historical control cohort in the current study. As the physician-staffed HEMS was introduced in the autumn of 2011, that year was excluded from data collecting.

Unconscious prehospital patients due to severe TBI were included in the study. Unconsciousness was defined as a Glasgow coma scale (GCS) score ≤ 8 [17] and was documented either on-scene, during transportation or by an on-call neurosurgeon on hospital admission. The ICD-10 hospital discharge diagnoses for traumatic brain injury and/or skull fracture (S06.2-S06.6, S06.8, S02.1) were used to identify the patients, and their patient records were cross-referenced with EMS and HEMS run-sheets. Patients with concomitant multiple injuries with the need for other than neurosurgical interventions were excluded, as were patients transferred from other hospitals.

Data collected included age, gender, mechanism of injury, GCS score and vital signs on-scene and on arrival at the ED, airway management, response and total mission times. Hypoxia was defined as an SpO_2 below 90% and hypotension was defined as a systolic blood pressure (SBP) below 90 mmHg. These definitions are consistent with the latest edition of the Brain Trauma Foundation's guidelines for prehospital management of traumatic brain injury [1]. For assessment of neurological outcome, a modified six-month Glasgow Outcome Score (GOS) was used [18, 19]. A GOS of 1 denoted death within six months, GOS 2–3 poor neurological outcome (need for assistance in activities of daily living) and GOS 4–5 good neurological recovery (independent life). Outcome evaluation was performed, or time of death was obtained, by the corresponding author, based on hospital patient records six months after the incident. If the outcome evaluation was unclear, the research team members reviewed the case and a joint decision was made.

Statistical analyses

Results are expressed as medians with ranges or percentages. The groups were compared using the chi-square or Fisher's exact test for categorical variables. Six-month survival is presented with Kaplan-Meier curves. Comparison between EMS and HEMS was made with the log-rank test.

Binary logistic regression analysis was used to predict good outcome. Variables of the univariate analysis with $p < 0.05$ were added to the multivariable analysis. Statistical significance was considered at a p-value less than 0.05. The data were analysed using IBM SPSS Statistics for Windows Version 21.0. Armonk, NY: IBM Corp. released 2012.

Results

During the study period (Periods 1 + 2) data from 181 patients in the EMS group and 85 patients in the HEMS group were available for neurological outcome analyses (Fig. 1). The baseline characteristics and the first recorded vital signs of the two cohorts were similar and are presented in Table 1.

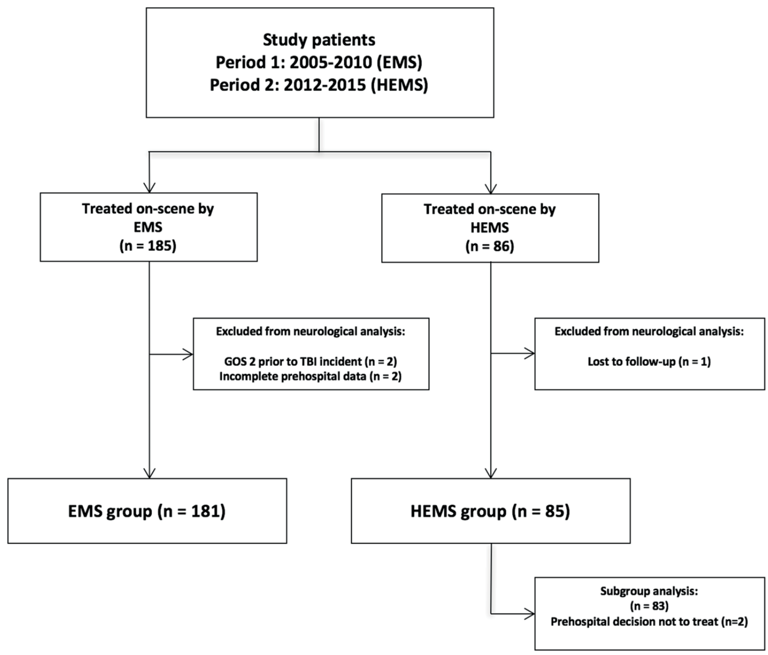

Fig. 1 Flow-chart

Table 1 Baseline characteristics

		Period 1: EMS		Period 2: HEMS		
		n = 181		*n* = 85		p-value
Age, years	(Median, Q_1-Q_3)	54	33–69	53	23–74	0.479
Gender, male	(n, %)	127	70	58	68	0.820
Mechanism of injury	(n, %)					0.288
Fall from ground level		79	43	32	38	
Traffic accident		41	23	29	34	
Fall from a height (> 2 m)		25	14	9	11	
Violence		14	8	6	7	
Other		4	2	4	5	
Unknown		18	10	5	6	
Primary GCS	(Median, Q_1-Q_3)	5	3–7	5	3–7	0.956
Primary vital parameters	(n/total, %)					
Hypoxia		32/170	19	18/84	21	0.369
Hypotension		7/174	4	4/84	5	0.514
Airway secured	(n, %)	29	16	81	95	< 0.001
Prehospital decision not to treat		–	–	2	2	
Vital parameters on arrival at the ED	(n/total, %)					
Hypoxia		18/173	10	2/84	2	0.024
Hypotension		7/179	4	4/85	5	0.750
Mission related times, minutes	(Median, Range)					
From dispatch to arrival on-scene						
1st EMS Unit on-scene		8	0–37	12	4–41	0.006
HEMS		–	–	23	6–85	
Total mission time		54	18–180	82	30–201	< 0.001

Good neurological outcome was more frequent in the HEMS group; 42% of the HEMS managed patients and 28% (p = 0.022) of the EMS managed patients had a good neurological recovery (GOS 4–5), living an independent life six months after the incident. There was a trend to higher survival (53% vs. 43%, Log Rank p = 0.066) in the HEMS group during the 6-month follow-up period, presented as Kaplan-Meier curves in Fig. 2. A prehospital decision not to treat was done by the attending HEMS physician on two patients. A subgroup Kaplan-Meier analysis with these two patients removed from the HEMS group resulted in higher survival (p = 0.045).

The logistic regression analysis is presented in Table 2. The airway was secured more frequently in the HEMS group (p < 0.001). Due to long distances, 10 patients were air transported to the ED in the HEMS group, while patient transport was mainly carried out by EMS ground vehicles with the physician escorting the patient. On arrival at the ED, patients in the HEMS group were less often hypoxic (p = 0.024). In univariate analysis HEMS-period, lower age and secured airway were

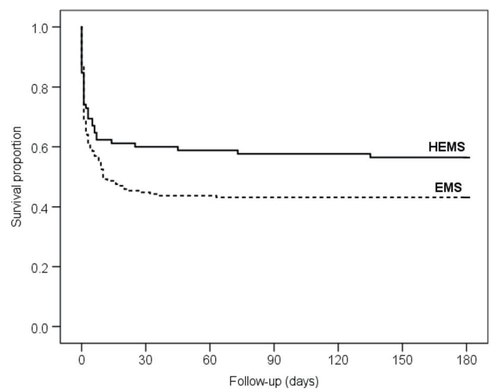

Fig. 2 Six-month survival according to EMS system (Log Rank p = 0.066)

Table 2 Univariate and multivariable logistic regression of six-month good outcome predictors

	Univariate			Multivariable		
	OR	95% CI	p-value	OR	95% CI	p-value
Period						
HEMS	1.87	1.09–3.21	0.022	2.46	0.89–6.84	0.083
EMS	1					
Age	0.95	0.93–0.96	< 0.001	0.95	0.93–0.96	< 0.001
Sex						
Male	1.78	0.99–3.19	0.055	Not entered		
Female	1					
GCS	1.07	0.97–1.18	0.183	Not entered		
Hypoxia						
On-scene	1			Not entered		
Not present	1.65	0.81–3.37	0.165			
Hypotension						
On-scene	1			Not entered		
Not present	2.26	0.48–10.72	0.303			
Airway						
Secured	1.89	1.12–3.19	0.017	0.71	0.27–1.88	0.486
Not secured	1					
Hypoxia						
At ER	1			Not entered		
Not present	2.12	0.69–6.54	0.193			
Hypotension						
At ER	1			Not entered		
Not present	2.28	0.48–10.78	0.299			

associated with good neurological outcome. In multivariable analysis lower age remained as a significant factor for good outcome.

Discussion

The introduction of a physician-staffed HEMS unit significantly decreased the proportion of hypoxic TBI patients and increased the number of patients with secured airways on hospital admission. This may have contributed to the observed improved neurological outcome during the HEMS period.

This supports our previous findings when evaluating mortality and neurological outcome of TBI patients in two regions with differently structured EMS systems [10].

The baseline characteristics of the two cohorts were similar, with no differences between the groups regarding gender, mechanism of injury or initial GCS. Only the mission-related time frames differed, since the response time and delay to hospital admission were longer in the HEMS group. In the HEMS group 10 patients were air transported to the ED, but as the total mission times in the HEMS group were longer, this result in our opinion excludes the impact of the air transport itself.

The principles for prehospital airway management of TBI patients are described in international guidelines: an airway should be established in patients who have severe TBI (GCS ≤ 8), who are unable to maintain an adequate airway or who are hypoxaemic despite supplemental oxygen [1]. The optimal way to secure the airway still remains controversial [20, 21]. With endotracheal intubation, if RSI is performed poorly, hypoxia and hypotension have been shown to have a negative effect on outcome of TBI patients [21–23]. In the present study, virtually all patients were intubated in the prehospital setting in the physician-staffed HEMS group, whereas only a few patients were intubated in the paramedic EMS group. In univariate analysis of the HEMS-period, securing the airway was associated with good neurological outcome. Anaesthetics were used by the HEMS physicians, while the paramedics were limited to the use of sedatives and opioids. This may have influenced on the observed difference in the rate of airway management procedures during the two periods.

In previous studies both hypoxaemia and hypotension have been shown to have a negative impact on TBI outcome [2, 5]. We found no difference in the on-scene occurrence of disturbances of these vital signs between the study groups. The proportion of hypotensive patients on arrival to the ED was similar in both groups. However, hypoxia was more common in the patients managed by the paramedic EMS. The likely explanation for this finding is the higher frequency of prehospital endotracheal intubation, controlled ventilation and more precise and invasive monitoring of the vital signs in the HEMS group.

Age has been demonstrated to be an important predictor of outcome after head injury. Older age has been shown to be an independent risk factor for higher mortality and poor functional outcome in TBI [24, 25]. In this study, in uni- and multivariate analysis of the HEMS-period lower age was associated with good neurological outcome.

Study limitations

This was a retrospective observational study and the following limitations should be considered when interpreting the results. The prehospital data were originally self-reported, could not be independently verified, and could therefore have been biased. Continuous data on vital signs covering the whole prehospital phase were not available; therefore, short-lived hypoxia or hypotension during the prehospital period cannot with certainty be excluded during either period. Due to the low rate of endotracheal intubation in the paramedic EMS group, parameters regarding ventilation could not be compared. The first CT scans were not evaluated using the Marshall classification. Neurosurgical and intensive care have advanced during the study period, which may also have affected the results and may to some extent account for the improved outcome. Outcome evaluation was based on patient record assessment without clinical examination or the help of a questionnaire. It is possible that the deaths occurring in the late stages of the follow-up period were unrelated to the prehospital index event, with secondary diseases or injury being the cause.

Conclusions

The introduction of a physician-staffed HEMS unit resulted in a beneficial impact on patient care reflected by a decreased incidence of prehospital hypoxia and an increased number of patients with secured airways. This may have contributed to the observed improved neurological outcome during the HEMS period. Further prospective multicentre studies with detailed data are needed to confirm the hypothesis that a physician-staffed HEMS has a positive impact on the outcome of TBI patients.

Abbreviations

ED: Emergency Department; EMS: Emergency Medical Services; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Score; HEMS: Helicopter Emergency Medical Service; RSI: Rapid Sequence Intubation; TBI: Traumatic Brain Injury

Acknowledgements

This study is dedicated to the memory of Janne Virta, M.D.

Availability of data and supporting materials

Please contact author for data requests.

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Declarations

The study was conducted in the the Pirkanmaa Hospital District, Finland.

Authors' contributions

TP: the concept and design of the study, acquisition and evaluation of the data and corresponding author. AK: the concept and design of the study, evaluation of the data and the manuscript. HH: statistical analyses. TS: evaluation of the data and the manuscript. JN: evaluation of the data and the manuscript. IV: evaluation of the data and the manuscript. AYH: evaluation of the data and the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the Regional Ethics Committee of the Pirkanmaa Hospital District (reference number R15158), permission to conduct the study was obtained from the Research Director of Tampere University Hospital and registered in ClinicalTrials.gov (Identifier NCT02659046, registered January 15th 2016).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

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PUBLICATION
IV

Prehospital on-scene anaesthetist treating severe traumatic brain injury patients is associated with lower mortality and better neurological outcome

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ORIGINAL RESEARCH **Open Access**

Prehospital on-scene anaesthetist treating severe traumatic brain injury patients is associated with lower mortality and better neurological outcome

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Abstract

Background: Patients with isolated traumatic brain injury (TBI) are likely to benefit from effective prehospital care to prevent secondary brain injury. Only a few studies have focused on the impact of advanced interventions in TBI patients by prehospital physicians. The primary end-point of this study was to assess the possible effect of an on-scene anaesthetist on mortality of TBI patients. A secondary end-point was the neurological outcome of these patients.

Methods: Patients with severe TBI (defined as a head injury resulting in a Glasgow Coma Score of ≤8) from 2005 to 2010 and 2012–2015 in two study locations were determined. Isolated TBI patients transported directly from the accident scene to the university hospital were included. A modified six-month Glasgow Outcome Score (GOS) was defined as death, unfavourable outcome (GOS 2–3) and favourable outcome (GOS 4–5) and used to assess the neurological outcomes. Binary logistic regression analysis was used to predict mortality and good neurological outcome. The following prognostic variables for TBI were available in the prehospital setting: age, on-scene GCS, hypoxia and hypotension. As per the hypothesis that treatment provided by an on-scene anaesthetist would be beneficial to TBI outcomes, physician was added as a potential predictive factor with regard to the prognosis.

Results: The mortality data for 651 patients and neurological outcome data for 634 patients were available for primary and secondary analysis. In the primary analysis higher age (OR 1.06 CI 1.05–1.07), lower on-scene GCS (OR 0.85 CI 0.79–0.92) and the unavailability of an on-scene anaesthetist (OR 1.89 CI 1.20–2.94) were associated with higher mortality together with hypotension (OR 3.92 CI 1.08–14.23). In the secondary analysis lower age (OR 0.95 CI 0.94–0.96), a higher on-scene GCS (OR 1.21 CI 1.20–1.30) and the presence of an on-scene anaesthetist (OR 1.75 CI 1.09–2.80) were demonstrated to be associated with good patient outcomes while hypotension (OR 0.19 CI 0.04–0.82) was associated with poor outcome.

Conclusion: Prehospital on-scene anaesthetist treating severe TBI patients is associated with lower mortality and better neurological outcome.

Keywords: Prehospital emergency care (MeSH), Emergency medical services (MeSH), Critical care (MeSH), Traumatic brain injury (MeSH), Airway management (MeSH), Endotracheal intubation (MeSH), Patient outcome assessment (MeSH), Glasgow outcome scale (MeSH)

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Background

The incidence of patients admitted to hospital with traumatic brain injury (TBI) in Europe is estimated to be 262/100,000, with average related mortality of 11/100,000 [1]. Approximately 10–20% of all TBIs are moderate or severe, requiring intensive care unit treatment [2, 3]. Severe traumatic brain injury is defined as a head injury resulting in a Glasgow Coma Score of ≤8 [4] and the prognosis for severe TBI is that one in two patients dies as a result or is severely affected as a result of the trauma [5, 6]. In large registry studies, TBI outcomes have been demonstrated to be strongly associated with demographic and trauma-related factors (i.e., age, motor score, pupillary reactivity and computed tomography classification) as well as with secondary factors (hypoxia and arterial hypotension primarily) in large registry studies [6–8].

Prehospital assessment and treatment is an important link in providing appropriate care [9] as the prognosis of patients with severe TBI strongly depends on early support of vital functions [10, 11]. In particular, prehospital prevention of hypotension and hypoxia by adequate treatment including a secured airway, normoventilation and prevention of aspiration is strongly associated with improved outcome [12–15].

The effect of advanced interventions by prehospital physicians on patient outcomes has been examined in only a few controlled studies. Increased survival has been found in patients with major trauma and in cardiac arrest patients [16]. In particular, patients with isolated TBI are also likely to benefit from a prehospital physician treating and preventing secondary brain injury insults [17]. Severe TBI patients treated by on-scene anaesthetists have been shown to have a better prognosis in our previous studies [18, 19]. Thus, the current study objective was to further analyse the previously gathered patient data using binary logistic regression analysis. The hypothesis was that interventions by prehospital anaesthetists would have a positive effect on severe TBI patient outcomes. The primary end-point was to evaluate the possible effect of an on-scene anaesthetist on mortality and as a secondary end-point, the neurological outcome in TBI patients.

Methods

Study setting

The prehospital treatment and outcomes of patients with severe TBI from 2005 to 2010 and 2012–2015 in two study locations (Helsinki and Uusimaa region and Pirkanmaa region, Finland) were determined in this retrospective cohort study. The Helsinki and Uusimaa area represents a 10-year continuous patient flow in a physician-staffed emergency medical service (EMS) system. The Pirkanmaa patient cohort was divided into two sections: 2005–2010 with no prehospital physician service and 2011–2015 after the implementation of a physician-staffed EMS unit. Previously gathered patient data, in conjunction with previously unused data (representing 18% of the total information), was further analysed using binary logistic regression analysis. The data covering 2011 were excluded as a physician-staffed helicopter emergency medical service (HEMS) was implemented in the Pirkanmaa Hospital District that year and impacted significantly on the local EMS. There were no dedicated medical directors in the Pirkanmaa area until 2010 and EMS crews consulted on-call hospital physicians for treatment guidelines.

The two present EMS systems, described in detail in previous publications [18, 19], serve a total of almost two million inhabitants and comprise basic life support, advanced life support and physician-staffed units. The physician-staffed units respond to medical emergencies as well as trauma calls. The prehospital physicians are anaesthesiologists with extensive experience in prehospital emergency medicine. All severe TBI patients in these regions are admitted to the region's single university hospital and receive immediate neurosurgical care according to the national guidelines [20].

The study protocol was approved by the Regional Ethics Committee of the Pirkanmaa Hospital District (No. R15158). Permission to conduct the study was obtained from the research directors of Tampere University Hospital and Helsinki University Hospital. The study was registered in ClinicalTrials.gov (Identifier NCT02659046) (originally on 15 January 2016 and then updated on 12 December 2017).

Definitions and data collection

Severe TBI was defined as a GCS score ≤ 8, occurring either on scene, during transportation or verified by an on-call neurosurgeon on admission to hospital [21]. Advanced airway management was defined as securing the airway with endotracheal intubation, a supraglottic airway device (laryngeal mask) or surgical airway. Hypoxia was defined as a SpO_2 of ≤90% and hypotension as a systolic blood pressure (SBP) of ≤90 mmHg. The definitions are consistent with the latest edition of the Brain Trauma Foundation's guidelines for the prehospital management of TBI [4].

Included patients were identified from the hospital records based on ICD-10 discharge diagnoses for TBI (S06.2-S06.6 and S06.8). The inclusion criterion for the study was severe, isolated TBI in patients transported directly from the accident scene to the university hospital. Non-Finnish citizens were excluded from the study since follow-up data were not available to perform a neurological outcome evaluation. Patients with multiple injuries and requiring surgical intervention (other than neurosurgery) were also excluded, as were those who were transferred from other hospitals (i.e., inter-hospital transfers).

Age, gender, response time, total prehospital time, mechanism of injury, Glasgow Coma Scale (GCS) score, advanced airway management and vital signs on scene and on arrival at the emergency department (ED) were reviewed and cross-referenced with EMS run sheets and ED documentation.

Mortality data were obtained from the national statistical authority, Statistics Finland. A neurological outcome evaluation was performed based on the hospital patient records up to 6 months after the incident. A modified six-month Glasgow Outcome Score (GOS) [22, 23] was used to assess the neurological outcomes. A GOS of 1 denoted death within 6 months, a GOS of 2–3 was indicative of a poor neurological outcome (i.e., needing assistance with daily living activities) and a GOS of 4–5 was suggestive of good neurological recovery (i.e., the ability to lead an independent life). If the outcome was unclear, the research team members reviewed the case and a joint decision was made.

Statistical methods

To describe general characteristics categorical variables are reported as percentage (%), while continuous variables are reported as median and range. Binary logistic regression analysis was used in univariate and multivariable models to predict mortality and a good neurological outcome. The evaluation was performed in the context of a prehospital environment using predictors that were of value in the prehospital treatment phase [17]. The following known conventional prognostic variables [5, 6] for TBI were available in the prehospital setting: age, on-scene GCS, hypoxia and hypotension. As per the hypothesis that treatment provided by an on-scene anaesthetist would be beneficial to TBI outcomes, physician was added as a potential predictive factor with regard to the prognosis. The results are presented as odds ratios (OR) with 95% confidence intervals. Statistical significance was considered to be a p-value of ≤0.050. The data were analysed using SPSS Statistics for Windows® version 21.0.

Results

Six hundred and sixty-three patients met the inclusion criterion. The mortality data for 651 patients and neurological outcome data for 634 patients were available for analysis (Fig. 1). Information on the sociodemographic patient characteristics, mechanism of injury, response and total prehospital times is provided in Table 1.

The median on-scene GCS was 5 (≤ 8 in 90%, 9–13 in 8% and 14–15 in 2% of the patients). Patients in the latter two groups deteriorated either on scene or during transportation and were consequently eligible for inclusion. Hypoxia was present on scene in 16% of the patients and hypotension was documented in 3% of them. The incidence of hypoxia (4%) and hypotension (4%)

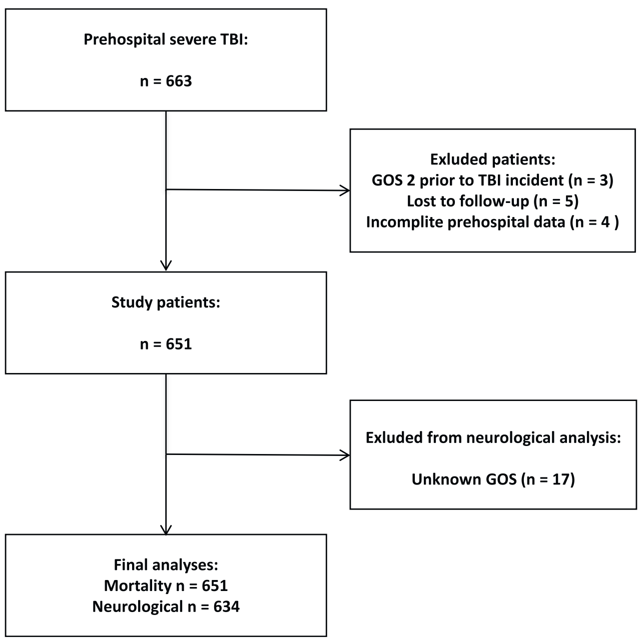

Fig. 1 Flowchart

Table 1 General characteristics

	Median / %	Q_1-Q_3
Age (y)	50	30–64
Male	74%	
Mechanism of injury		
Fall	38%	
Traffic accident	24%	
Fall from a height (> 2 m)	12%	
Violence	9%	
Other	7%	
Unknown	9%	
1st EMS Unit on scene (minutes)	8	5–12
Total mission time (minutes)	69	53–92
GCS on-scene (range)	5 (3–15)	
Hypoxia		
On-scene	16%	
ER	4%	
Hypotension		
On-scene	3%	
ER	4%	
Physician	72%	
Airway secured	74%	

GCS Glasgow Coma Score, *ER* Emergency Room
Hypoxia SpO_2 of ≤90%, *Hypotension* systolic blood pressure (SBP) of ≤90

was similar on arrival at the ED. An anaesthetist was present on scene in 72% of the cases and advanced airway management was performed in 74% of the patients. The airway of 97% of the patients was secured in the prehospital setting when an on-scene anaesthetist was present and in 16% of the patients who were not treated by a physician.

Higher age, lower on-scene GCS and the unavailability of an on-scene anaesthetist were associated with higher mortality in univariate analysis. The same variables (age, GCS, an on-scene anaesthetist), together with hypotension, were found to be significant factors for mortality in multivariable analysis (Table 2).

Lower age, a higher on-scene GCS and the presence of an on-scene anaesthetist were linked to good neurological outcomes in univariate analysis. Following multivariable analysis, all of these factors were demonstrated to be significantly associated with good patient outcomes (age, GCS, an on-scene anaesthetist), while hypotension was associated with poor outcomes (Table 3).

Discussion

In this retrospective observational study, prehospital on-scene anaesthetist treating severe TBI patients was associated with lower mortality and better neurological outcome.

Table 2 Mortality regression analyses

	Univariate			Multivariable		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age	1.06	1.05–1.07	< 0.001	1.06	1.05–1.07	< 0.001
GCS On-scene	0.91	0.85–0.96	0.002	0.85	0.79–0.92	< 0.001
Hypoxia						
Not present	1					
On-scene	1.31	0.84–2.03	0.230	0.93	0.55–1.59	0.792
Hypotension						
Not present	1					
On-scene	2.03	0.78–5.31	0.149	3.92	1.08–14.23	0.038
Physician						
Not present	2.03	1.44–2.88	< 0.001	1.89	1.20–2.94	0.005
On-scene	1					

GCS Glasgow Coma Score, *OR* Odds ratio, *CI* Confidence Interval
Hypoxia SpO_2 of ≤90%, *Hypotension* systolic blood pressure (SBP) of ≤90 mmHg

The results supports our previous finding following an evaluation of mortality and neurological outcomes in TBI patients [18, 19]. However, there is lack of consensus on the impact of physician-staffed EMS on trauma patients in the literature and results from existing studies are inconclusive [16, 17, 24–27].

Early definitive airway control has become an established principle in the management and resuscitation of critically injured patients. This practise is considered to be the standard of care, particularly in patients with head trauma as hypoxemia and hypercapnia can worsen brain injury [28].

Prehospital treatment (i.e., ensuring a secured airway, preventing hypoxemia and enabling controlled ventilation) administered by an on-scene anaesthetist was associated

Table 3 Good neurological outcome regression analyses

	Univariate			Multivariable		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age	0.95	0.94–0.96	< 0.001	0.95	0.94–0.96	< 0.001
GCS On-scene	1.15	1.08–1.22	< 0.001	1.21	1.20–1.30	< 0.001
Hypoxia						
Not present	1					
On-scene	0.66	0.41–1.05	0.079	1.05	0.60–1.83	0.863
Hypotension						
Not present	1					
On-scene	0.44	0.14–1.34	0.148	0.19	0.04–0.82	0.026
Physician						
Not present	0.51	0.35–0.74	< 0.001	0.57	0.36–0.92	0.020
On-scene	1					

GCS Glasgow Coma Score, *OR* Odds ratio, *CI* Confidence Interval
Hypoxia SpO_2 of ≤90%, *Hypotension* systolic blood pressure (SBP) of ≤90 mmHg

with the observed lower mortality and improved neurological outcome in patients in the current study.

Virtually all patients with severe TBI who were treated by an on-scene anaesthetist had their airways secured in the prehospital setting. This concurs with the finding of a recent study by Gellerfors et al., in which it was shown that prehospital tracheal intubation was completed rapidly, with high success rates and a low incidence of complications when performed by experienced anaesthetists [29].

It has been suggested that the dispatch of physician-staffed EMS could increase on-scene time (OST). It is likely that different prehospital treatment strategies (i.e., “scoop and run” and “stay and play”) and interventions (i.e., airway management performed on scene) influence the OST and, depending on the injury profile, impact on patient outcomes. The literature is also inconclusive regarding the effect of prehospital timeframes on the outcomes of patients with severe TBI [17, 24, 30]. Unfortunately, reliable prehospital OST data were not available in our study.

Hypotension has been shown to have a negative impact on TBI outcomes in previous studies [10, 12]. It has been suggested that SBP values higher than 90 mmHg may benefit patients with isolated, severe TBI [31–35]. Hypotension, or the lack of it, was seen to have a significantly negative impact on survival (i.e., increased mortality) and a significantly positive impact on neurological outcomes, respectively, on multivariable analysis in the current study.

When considering other individual prognostic factors, age is an important predictor of outcome after brain trauma. The elderly (typically defined as age higher than 64–70 years) have higher mortality and worse functional outcomes compared to younger patients with the oldest patients having the poorest outcomes [36–39]. A GCS score of 3 at presentation is associated with very poor outcomes. Similarly, an increase in mortality and the worsening of neurological outcomes has been demonstrated in patients with a GCS of ≤8 [40–42]. A prehospital assessment of the GCS has been found to be an important and reliable indicator of the severity of TBI and should ideally be measured prior to the administration of sedative or paralytic agents [4]. The assessment should be repeatedly conducted to determine improvement or deterioration over time [4]. The results of the current study are comparable with these earlier findings.

Strengths and limitations

Strengths of the current study were that this was a population-based study and that all primary EMS mission patients with severe TBI were treated and cared for in the study university hospitals. The included patients were recruited based on a confirmed diagnosis of severe TBI on discharge. Lastly, the mortality data were obtained from the national statistical authority, Statistics Finland, which publishes official causes of death statistics.

A major limitation of this study is that, due to the design, the improved patient outcome can only be associated with the treatment provided by prehospital physician. To obtain prehospital data and timeframes, the study only included patients from primary EMS missions. Also, neurosurgical and intensive care advances were made as well as a new HEMS unit was implemented to one of the EMS system during the study period, all which should be taken into consideration when interpreting the results. The prehospital data were not originally documented for the purpose of this study, could not be independently verified and thus could have been biased. Continuous data on patient vital signs for the entire prehospital phase were unavailable. Accordingly, transient hypoxia or hypotension during the prehospital period could not be excluded with absolute certainty. Similarly, an eye assessment (pupils) was not recorded for all of the patients. Thus, all of the prognostic variables used in previous studies were not available for analysis in this study. It is possible that the deaths that occurred in the late stages of the follow-up period were unrelated to the prehospital index event, i.e., secondary disease or injury was the cause. The outcome evaluation was based on an evaluation of the patient records by without the ability to perform a clinical examination or with the help of a questionnaire.

Conclusion

Prehospital on-scene anaesthetist treating severe TBI patients is associated with lower mortality and better neurological outcome.

Appendix

Table 4 Comparison of the patients between the study locations

	Helsinki and Uusimaa		Tampere		
	Median / %	Q_1-Q_3	Median / %	Q_1-Q_3	*p*-value
GCS On-scene	4	3–7	5	3–7	0.139
Hypoxia					
On-scene	14.1%		18.2%		0.171
ER	1.4%		7.8%		< 0.001
Hypotension					
On-scene	3.3%		4.2%		0.558
ER	1.9%		4.3%		0.088

GCS Glasgow Coma Score, *ER* Emergency Room
Hypoxia SpO_2 of ≤90%, *Hypotension* systolic blood pressure (SBP) of ≤90

Abbreviations
ED: Emergency department; EMS: Emergency medical services; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Score; HEMS: Helicopter emergency medical service; TBI: Traumatic brain injury

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Availability of data and materials
Please contact author for data requests.

Declarations
The study was conducted in the Helsinki and Uusimaa Hospital District, Finland and in the Pirkanmaa Hospital District, Finland.

Authors' contributions
TP the concept and design of the study, acquisition and evaluation of the data and corresponding author. JN the concept and design of the study, evaluation of the data and the manuscript. HH statistical analyses. TS evaluation of the data and the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The study protocol was approved by the Regional Ethics Committee of Pirkanmaa Hospital District (No. R15158). Permission to conduct the study was obtained from the research directors of Tampere University Hospital and Helsinki University Hospital. The study was registered in ClinicalTrials.gov (Identifier NCT02659046) (originally on 15 January 2016 and then updated on 12 December 2017).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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